Supporting Information for

A Retro-Staudinger Cycloaddition: Mechanochemical Cycloelimination of a β-Lactam Mechanophore

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I. General Experimental Details

Reagents from commercial sources were used without further purification unless otherwise stated. ^{13}C-labeled propargyl alcohol was purchased from Cambridge Isotope Laboratories. Dry THF was obtained from a solvent purification system equipped with activated alumina columns and stored over 3Å molecular sieves. Methyl acrylate was passed through a short plug of basic alumina to remove inhibitor immediately prior to use. All reactions were performed under a N_2 atmosphere unless specified otherwise. NMR spectra were recorded using a Varian 500 or 600 MHz spectrometer. All ^{1}H NMR experiments are reported in δ units, parts per million (ppm), and were measured relative to the signals for residual acetone (2.05 ppm), benzene (7.16 ppm), or DMSO (2.50 ppm) in deuterated solvent. All ^{13}C NMR spectra were measured in deuterated solvents and are reported in ppm relative to the signals for residual acetone (206.26 and 29.84 ppm), DMSO (39.52 ppm), or benzene (128.06 ppm). Mass spectra were obtained through the Mass Spectrometry Laboratory, School of Chemical Sciences, University of Illinois. Analytical gel permeation chromatography (GPC) was performed using a Waters 1515 Isocratic HPLC module equipped with a Waters (2998) Photodiode Array Detector, a Waters (2414) Refractive Index Detector, a Waters (2707) 96-well autosampler, and a series of 4 Waters HR Styragel columns (7.8 X 300 mm, HR1, HR3, HR4, and HR5) in THF at 30 °C and a flow rate of 1 mL/min. Molecular weights and molecular weight distributions were calculated relative to linear polystyrene standards. UV-Vis absorption spectra were recorded on a Shimadzu UV-2401PC spectrometer. Ultrasound experiments were performed using a Vibra Cell 505 liquid processor equipped with a 0.5'' diameter solid probe from Sonics and Materials. Suslick cells were fabricated by the School of Chemical Sciences Glass Shop at the University of Illinois. A Neslab CC 100 immersion cooler equipped with a Cryotrol temperature controller was used to maintain a constant-temperature bath for sonication experiments.

II. End-Group Analysis of Polymers Using ^{1}H NMR Spectroscopy

The dynamic range problem in FT-NMR[1] results from, in part, the deficiency of the analog-to-digital converter which cannot properly digitize weak signals in the presence of very strong signals. Typically, this presents an issue with small sample quantities and/or use of non-deuterated solvents (e.g., H_2O) where the solvent signal is much more intense than the analyte signals. However, end-group analysis of high molecular weight polymers can similarly suffer from this problem. In the present work, ^{1}H NMR spectra of polymer samples, where analysis of end-groups or chain-centered moieties was a priority, were acquired with presaturation of the methyl ester of poly(methyl acrylate) (3.65 ppm in Acetone-d_6). This procedure resulted in higher quality spectra with respect to the relatively weak signals of the end-groups or chain-centered units with improved baselines and elimination of artifacts.

III. GPC Traces of 1 and Control 3 Subjected to Ultrasonication

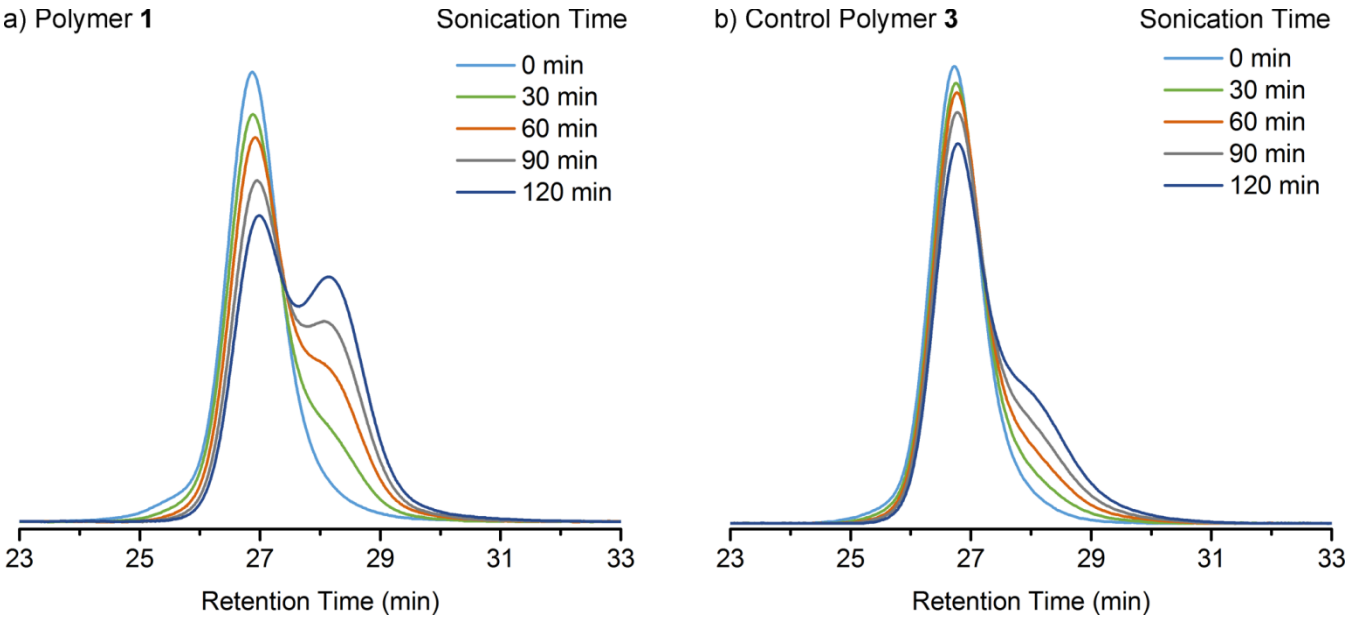


Figure S1. GPC chromatograms recorded using a refractive index detector for (a) chain-centered β-lactam polymer **1** and (b) chain-centered control polymer **3** subjected to pulsed ultrasonication for 0–120 min.

IV. UV-Vis Spectra of 1 and Chain-End Control 2 from GPC

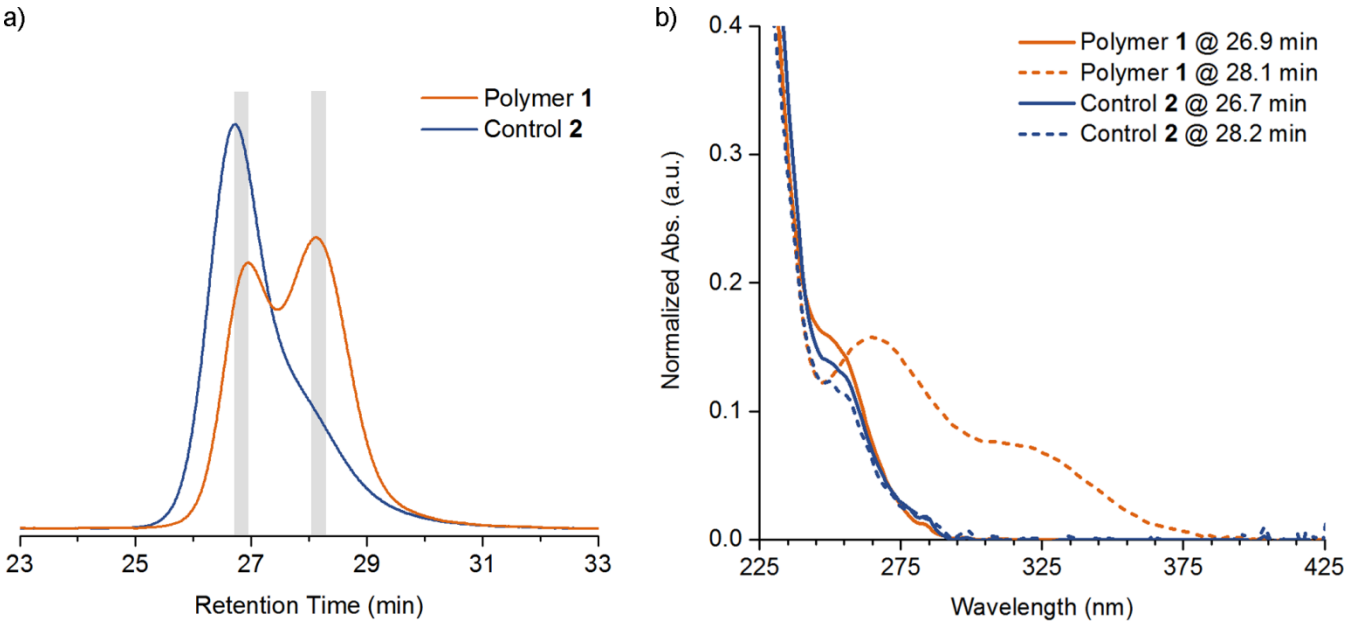


Figure S2. (a) GPC chromatograms recorded using a refractive index detector for polymer **1** and chain-end control polymer **2** after ultrasonication for 180 min. (b) UV-Vis spectra extracted from GPC measurements at retention times indicated by the grey shaded regions in (a) corresponding to the pristine polymers (solid lines) and the product of mechanochemical chain cleavage (dashed lines).

V. ^{1}H NMR Spectra of Polymer 1 and Model Compound 5

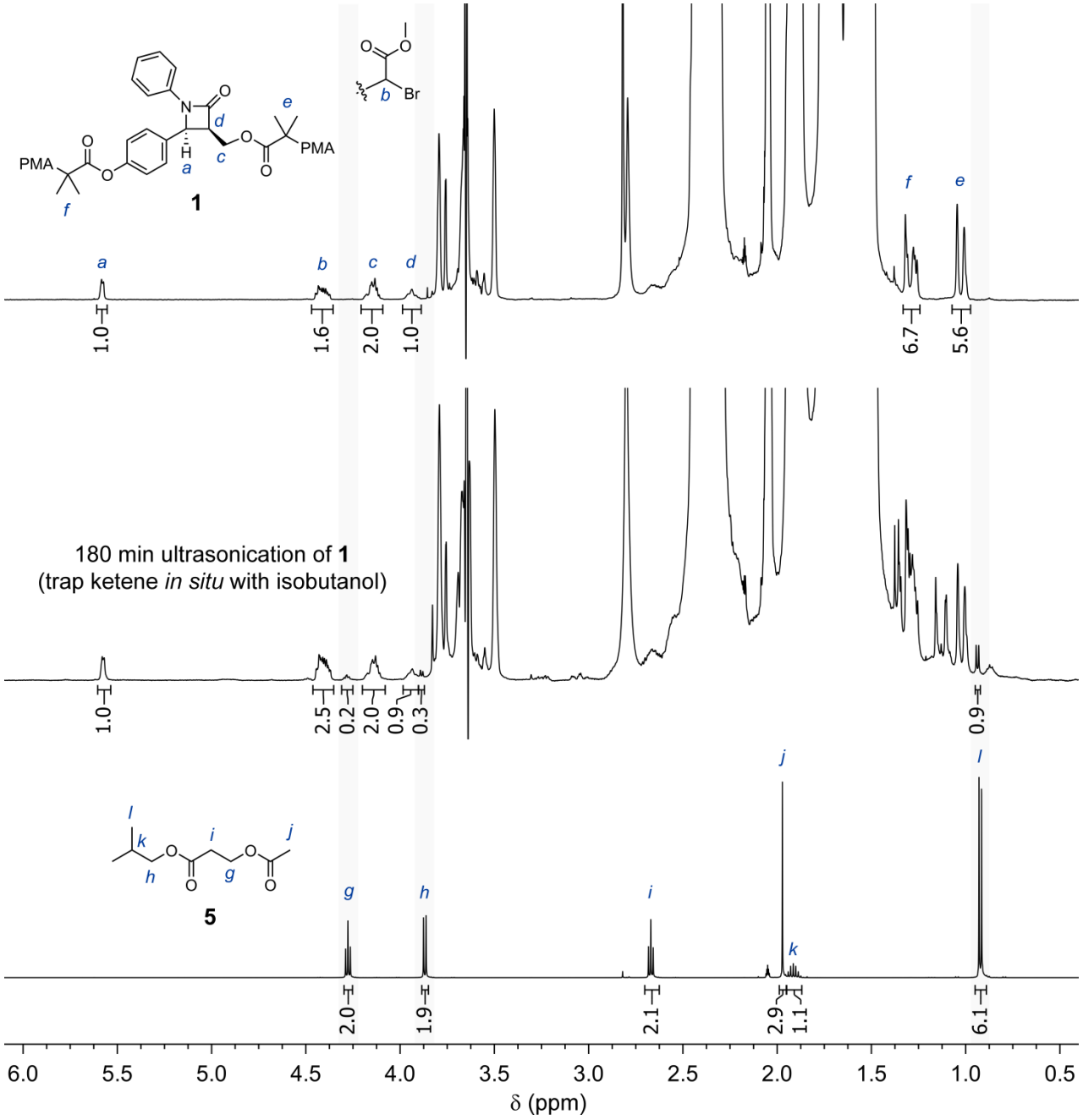


Figure S3. ^{1}H NMR spectra (500 MHz, acetone-d_6) of chain-centered β-lactam polymer **1** before (*top*) and after (*middle*) ultrasonic irradiation for 180 min in the presence of a large excess of isobutanol. After ultrasonication, several new signals indicative of the formation of an isobutyl propionate end-group via reaction of a ketene intermediate are evident at 4.28 (appt t, J = 6.2 Hz), 3.89 (d, J = 6.4 Hz), and 0.94 (d, J = 6.7 Hz) ppm. These peaks are consistent with resonances at 4.28 (t, J = 6.3 Hz), 3.87 (d, J = 6.6 Hz), and 0.92 (d, J = 6.7 Hz) ppm (labeled *g*, *h*, and *l*, respectively) in the spectrum of model compound **5** (*bottom*).

VI. ^{1}H NMR Spectra of Chain-End Control Polymer 2

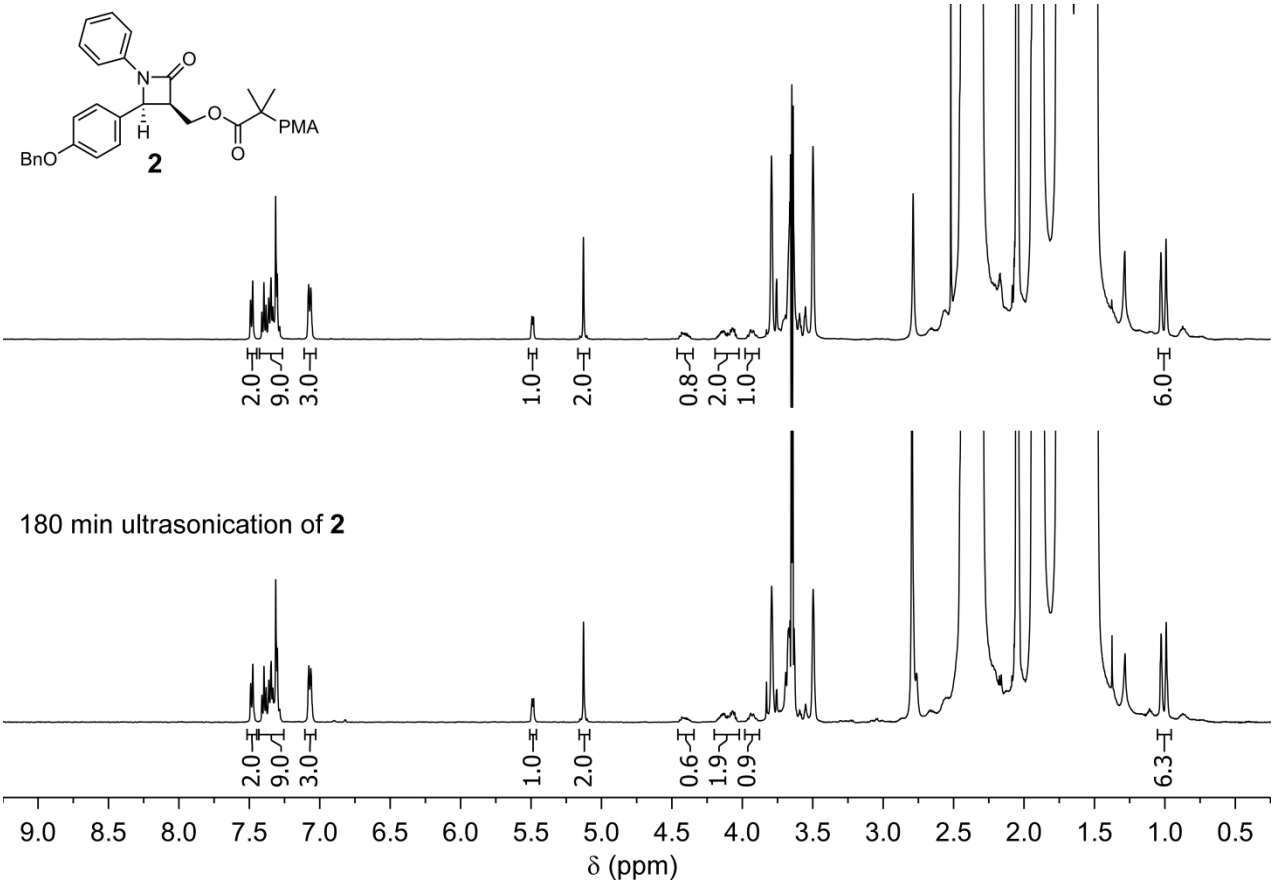


Figure S4. ^{1}H NMR spectra (500 MHz, acetone-d_6) of chain-end control polymer **2** before (*top*) and after (*bottom*) ultrasonic irradiation for 180 min. The spectra are essentially identical, indicating that mechanical force is indeed responsible for activation of the β-lactam mechanophore in **1** during ultrasonication.

VII. ^{13}C NMR Spectra of ^{13}C-Labeled Polymers and Model Compound 5

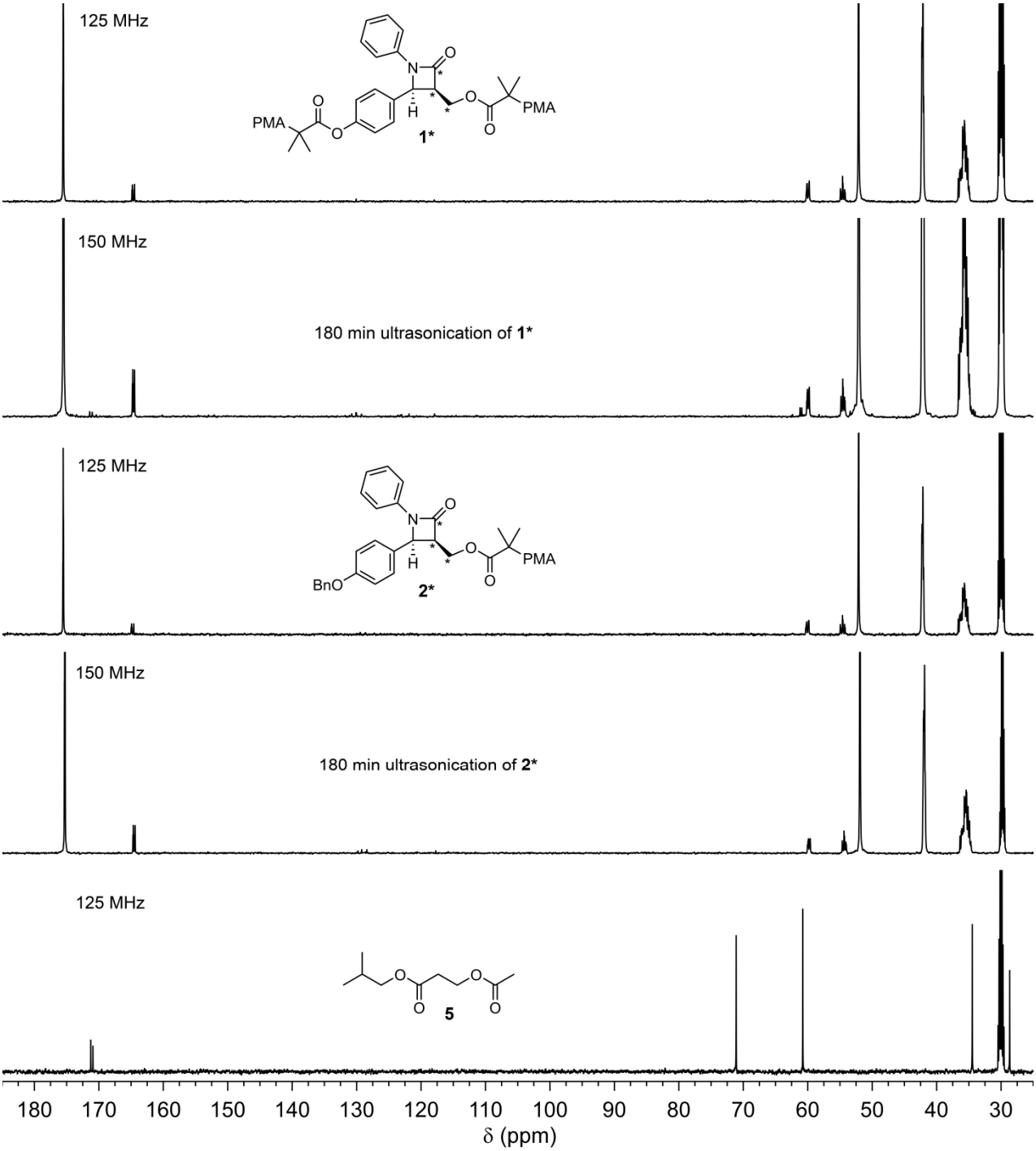


Figure S5. ^{13}C NMR spectra in acetone-d_6 of $^{13}C_3$-labeled polymer **1*** and chain-end control polymer **2*** before and after ultrasonic irradiation for 180 min in the presence of a large excess of isobutanol. The appearance of peaks consistent with model compound **5** after ultrasonication is only observed for polymer **1*** containing a chain-centered β-lactam mechanophore. The three carbon atoms of **1*** and **2*** derived from propargyl alcohol were ^{13}C-labeled.

VIII. GPC Traces of ^{13}C-Labeled Polymers 1* and 2* Before and After Ultrasonication

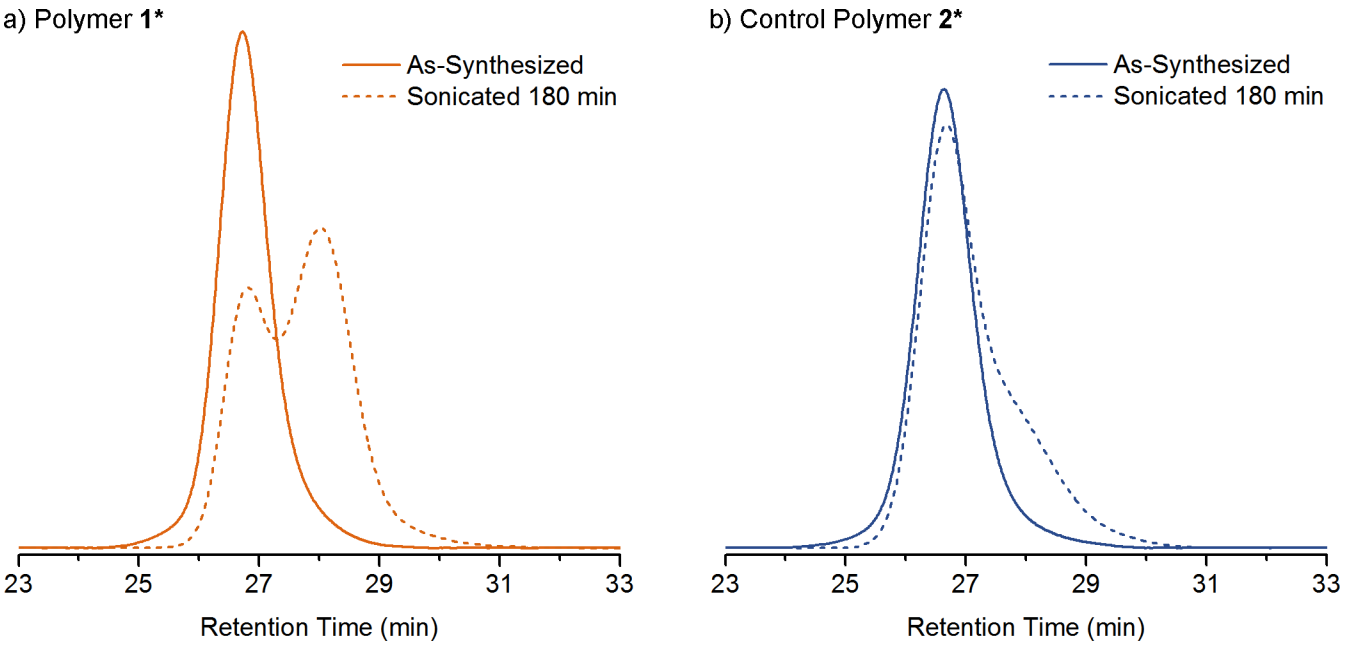
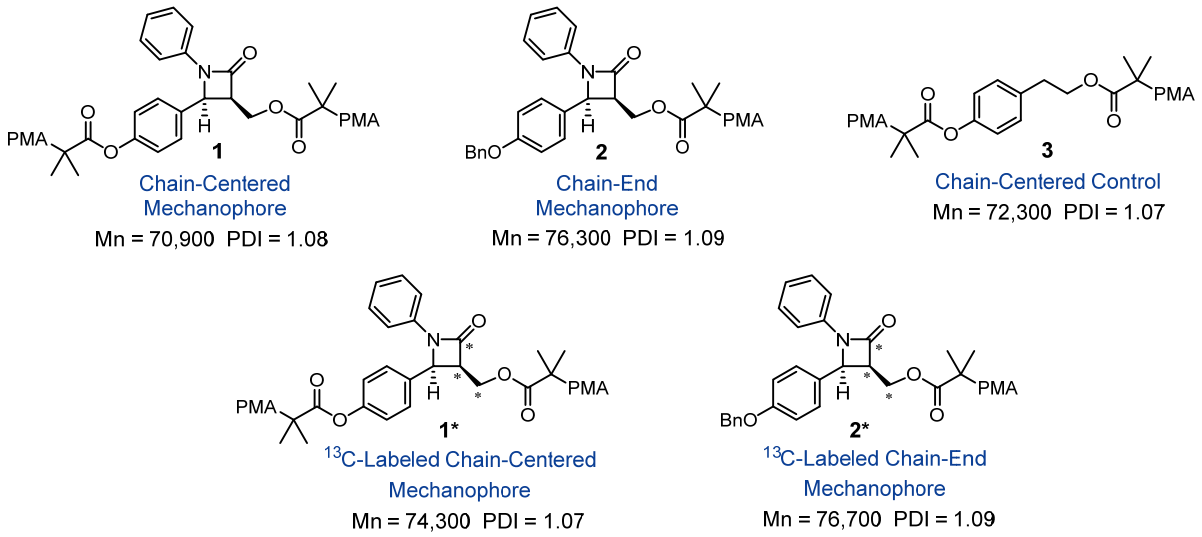
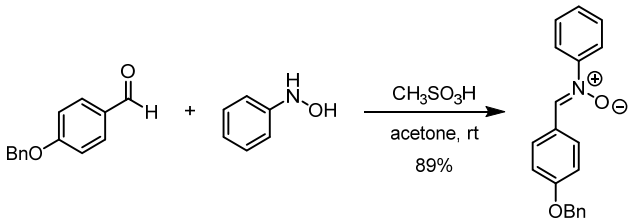


Figure S6. GPC chromatograms recorded using a refractive index detector for (a) polymer **1*** and (b) chain-end control polymer **2*** before and after pulsed ultrasonic irradiation for 180 min.

IX. Chart of All Polymers Studied with Molecular Weights and PDIs

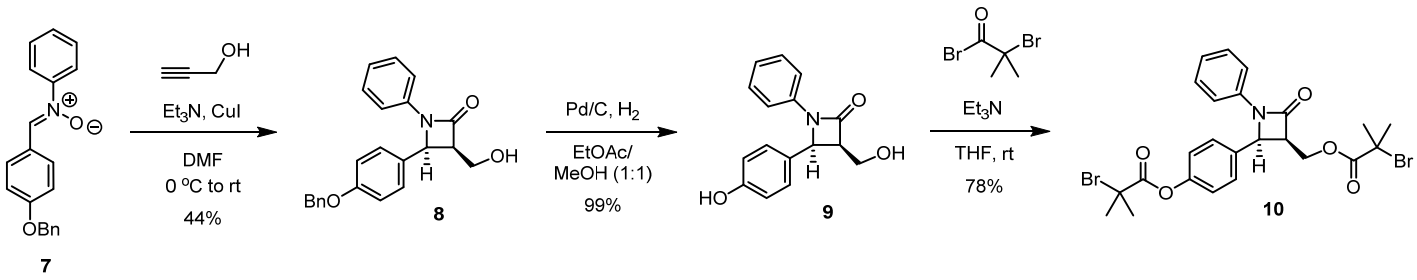


X. Synthetic Procedures



7

***N*-Phenyl-α-(4-benzyloxyphenyl)nitrone (7)**. *N*-Phenylhydroxylamine[2] (1.12 g, 10.3 mmol) and 4-(benzyloxy)benzaldehyde (2.16 g, 10.2 mmol) were dissolved in acetone (10 mL) in a 25 mL round bottom flask equipped with a stir bar and septum. One drop of methanesulfonic acid was added and the reaction mixture was stirred at room temperature. After 1 h, the solution was cooled in an ice bath and the precipitated solid was collected by vacuum filtration and washed with cold acetone to provide the title compound as a white powder (2.76 g, 89%). ^{1}H NMR (500 MHz, DMSO-d_6) δ: 5.20 (s, 2H), 7.11–7.20 (m, 2H), 7.31–7.37 (m, 1H), 7.37–7.44 (m, 2H), 7.45–7.58 (m, 5H), 7.85–7.94 (m, 2H), 8.43 (s, 1H), 8.46–8.53 (m, 2H) ppm. ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ: 69.4, 114.7, 121.3, 124.2, 127.9, 128.0, 128.5, 129.0, 129.5, 130.9, 132.9, 136.6, 148.4, 159.9 ppm. HRMS (ESI, *m*/*z*): calcd for $[C_{20}H_{18}NO_2]^+$ $(M+H)^+$, 304.1338; found, 304.1339.



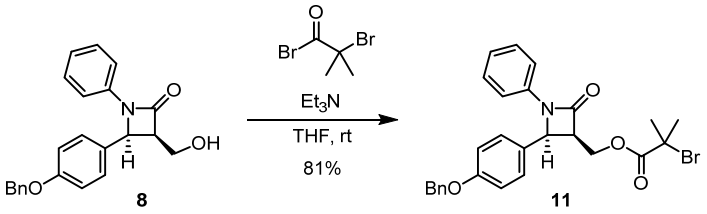
7 **8** **9** **10**

***cis*-4-(4-Benzyloxyphenyl)-3-hydroxymethyl-1-phenylazetidin-2-one (8)**. β-Lactams were synthesized via a Cu-catalyzed Kinugasa reaction following a modified procedure by Basak *et al.*[3] CuI (1.44 g, 7.56 mmol) was added to a 50 mL Schlenk flask equipped with a stir bar and a septum. The flask was evacuated and backfilled with nitrogen (3x) followed by the addition of DMF (25 mL) and triethylamine (1.05 mL, 7.53 mmol) via syringe. The flask was cooled in an ice bath followed by the dropwise addition of propargyl alcohol (0.44 mL, 7.6 mmol). After stirring for 15 min, nitrone **7** (1.14 g, 3.76 mmol) was added as a solid under a flow of nitrogen, the flask was re-sealed with a septum, and any remaining solid was washed down with addition DMF (5 mL). After stirring at room temperature overnight, the reaction mixture was poured into water (100 mL) and filtered through a short pad of celite. The bed was washed thoroughly with ethyl acetate (200 mL) and the aqueous layer was discarded. The organic fraction was washed with water (50 mL), 10% $NaHSO_4$ (50 mL), 10% $NaHCO_3$ (50 mL), and brine (50 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography (20–60% EtOAC/hexanes) to provide the title compound as an

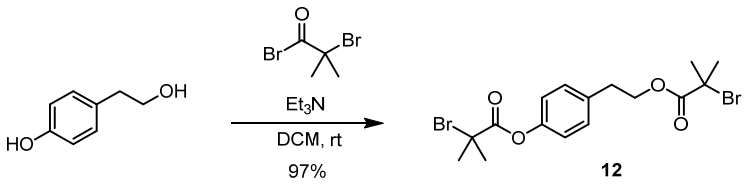
off-white solid (600 mg, 44%). R_f = 0.22 (EtOAc:hexane 1:1). ^{1}H NMR (500 MHz, Acetone-d_6) δ: 3.39 (dd, *J* = 5.5, 4.6 Hz, 1H), 3.48 (ddd, *J* = 11.4, 8.3, 5.5 Hz, 1H), 3.67 (dt, *J* = 11.3, 4.9 Hz, 1H), 3.83 (dt, *J* = 8.3, 5.5 Hz, 1H), 5.10 (s, 2H), 5.39 (d, *J* = 5.9 Hz, 1H), 7.00–7.06 (m, 3H), 7.23–7.36 (m, 7H), 7.36–7.43 (m, 2H), 7.46–7.52 (m, 2H) ppm. ^{13}C{^{1}H} NMR (125 MHz, Acetone-d_6) δ: 57.9, 58.0, 58.4, 70.6, 115.6, 117.8, 124.3, 128.2, 128.7, 128.8, 129.4, 129.6, 129.9, 138.4, 139.1, 159.8, 166.4 ppm. HRMS (ESI, *m*/*z*): calcd for $[C_{23}H_{22}NO_3]^+$ $(M+H)^+$, 360.1600; found, 360.1600.

***cis*-4-(4-Hydroxyphenyl)-3-hydroxymethyl-1-phenylazetidin-2-one (9)**. β-Lactam **8** (428 mg, 1.19 mmol) and 10% Pd/C (81.3 mg) were combined with ethyl acetate (12 mL) and methanol (12 mL) in a 100 mL round bottom flask equipped with a stir bar and septum. The flask was purged with nitrogen and then H_2 was introduced by balloon and the mixture was stirred at room temperature. After 10 h, the reaction mixture was filtered through a pad of celite and silica gel and washed thoroughly with ethyl acetate. The solvent was removed under reduced pressure to afford the title compound as a beige solid (317 mg, 99%). R_f = 0.29 (EtOAc:hexane 7:3). ^{1}H NMR (500 MHz, Acetone-d_6) δ: 3.38 (t, *J* = 5.1 Hz, 1H), 3.48 (ddd, *J* = 11.3, 8.2, 5.4 Hz, 1H), 3.66 (dt, *J* = 11.4, 5.0 Hz, 1H), 3.80 (dt, *J* = 8.2, 5.5 Hz, 1H), 5.34 (d, *J* = 5.8 Hz, 1H), 6.79–6.89 (m, 2H), 7.03 (tt, *J* = 6.7, 1.9 Hz, 1H), 7.14–7.22 (m, 2H), 7.22–7.33 (m, 4H), 8.44 (s, 1H) ppm. ^{13}C{^{1}H} NMR (125 MHz, Acetone-d_6) δ: 57.9, 58.1, 58.4, 116.3, 117.8, 124.2, 126.6, 129.5, 129.8, 139.2, 158.2, 166.5 ppm. HRMS (ESI, *m*/*z*): calcd for $[C_{16}H_{16}NO_3]^+$ $(M+H)^+$, 270.1130; found, 270.1143.

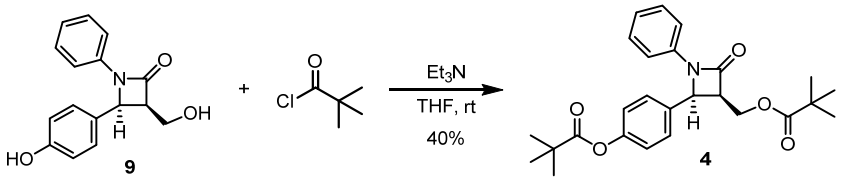
***cis*-4-(4-(2-bromoisobutyroxy)phenyl)-3-(2-bromoisobutyroxy)methyl-1-phenylazetidin-2-one (10)**. β-Lactam **9** (143 mg, 531 μmol) was dissolved in dry THF (4 mL) in an oven-dried 10 mL round bottom flask equipped with a stir bar and a septum. Triethylamine (152 μL, 1.09 mmol) was added via syringe followed by the dropwise addition of α-bromoisobutyryl bromide (135 μL, 1.09 mmol). After stirring at room temperature overnight, the reaction mixture was filtered through a pad of celite and silica gel, washing thoroughly with ethyl acetate. The filtrate was concentrated under reduced pressure and the crude product was purified by column chromatography (7–50% EtOAC/hexanes) to provide the title compound as a white solid (236 mg, 78%). R_f = 0.41 (EtOAc:hexane 3:7). ^{1}H NMR (500 MHz, Benzene-d_6) δ: 1.63 (s, 3H), 1.70 (s, 3H), 1.72 (s, 6H), 3.41 (dt, *J* = 9.3, 5.4 Hz, 1H), 3.80 (dd, *J* = 11.9, 9.3 Hz, 1H), 4.16 (dd, *J* = 11.9, 5.1 Hz, 1H), 4.37 (d, *J* = 5.9 Hz, 1H), 6.77–6.92 (m, 5H), 6.96–7.03 (m, 2H), 7.31–7.36 (m, 2H) ppm. ^{13}C{^{1}H} NMR (125 MHz, Benzene-d_6) δ: 30.4, 30.4, 30.6, 30.7, 53.7, 55.6, 55.8, 56.7, 60.4, 117.2, 121.8, 124.2, 128.4, 129.4, 132.0, 138.1, 151.1, 162.8, 169.7, 170.6 ppm. HRMS (ESI, *m*/*z*): calcd for $[C_{24}H_{26}Br_2NO_5]^+$ $(M+H)^+$, 566.0178; found, 566.0193.



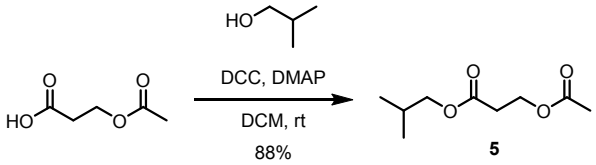
***cis*-4-(4-Benzyloxyphenyl)-3-(2-bromoisobutyroxy)methyl-1-phenylazetidin-2-one (11)**. β-Lactam **8** (62.7 mg, 174 μmol) was dissolved in dry THF (2 mL) in an oven-dried 10 mL round bottom flask equipped with a stir bar and a septum. Triethylamine (56 μL, 400 μmol) was added via syringe followed by the dropwise addition of α-bromoisobutyryl bromide (43 μL, 350 μmol). After stirring at room temperature overnight, the reaction mixture was concentrated under reduced pressure and the crude product was purified by column chromatography (7–50% EtOAC/hexanes) to provide the title compound as a white solid (72 mg, 81%). R_f = 0.54 (EtOAc:hexane 3:7). ^{1}H NMR (500 MHz, Benzene-d_6) δ: 1.63 (s, 3H), 1.69 (s, 3H), 3.42 (dt, *J* = 9.0, 5.5 Hz, 1H), 3.87 (dd, *J* = 11.8, 9.1 Hz, 1H), 4.22 (dd, *J* = 11.8, 5.2 Hz, 1H), 4.42 (d, *J* = 5.8 Hz, 1H), 4.59 (s, 2H), 6.65–6.72 (m, 2H), 6.77–6.87 (m, 3H), 6.98–7.04 (m, 2H), 7.04–7.09 (m, 1H), 7.09–7.15 (m, 2H), 7.17–7.21 (m, 2H), 7.41–7.46 (m, 2H) ppm. ^{13}C{^{1}H} NMR (125 MHz, Acetone-d_6) δ: 31.1, 54.4, 56.9, 57.6, 61.3, 70.6, 116.0, 118.0, 124.6, 127.3, 128.6, 128.8, 129.4, 129.5, 130.0, 138.3, 138.9, 160.0, 164.3, 171.4 ppm. HRMS (ESI, *m/z*): calcd for $[C_{27}H_{27}BrNO_4]^+$ $(M+H)^+$, 508.1123; found, 508.1128.



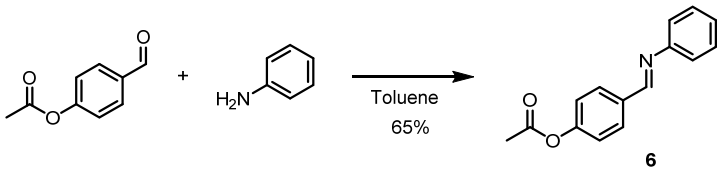
4-(2-(2-bromoisobutyroxy)ethyl)phenyl 2-bromoisobutyrate (12). An oven-dried 50 mL round bottom flask equipped with a stir bar and a septum was charged with 4-(2-hydroxyethyl)phenol (497 mg, 3.60 mmol) and dissolved in DCM (23 mL). Triethylamine (1.10 mL, 7.89 mmol) was added via syringe followed by the dropwise addition of α-bromoisobutyryl bromide (980 μL, 7.93 mmol). After stirring at room temperature overnight, the reaction mixture was filtered through a pad of celite and silica gel, washing thoroughly with DCM. The filtrate was concentrated under reduced pressure and the crude product was purified by column chromatography (5–40% EtOAC/hexanes) to provide the title compound as a white solid (1.53 g, 97%). R_f = 0.69 (EtOAc:hexane 3:7). ^{1}H NMR (500 MHz, Acetone-d_6) δ: 1.88 (s, 6H), 2.07 (s, 6H), 3.03 (t, *J* = 6.6 Hz, 2H), 4.39 (t, *J* = 6.6 Hz, 2H), 7.07–7.17 (m, 2H), 7.35–7.44 (m, 2H) ppm. ^{13}C{^{1}H} NMR (125 MHz, Acetone-d_6) δ: 31.0, 31.1, 34.9, 57.3, 57.4, 67.1, 122.1, 131.2, 137.1, 150.7, 170.8, 171.9 ppm. HRMS (ESI, *m/z*): calcd for $[C_{16}H_{21}Br_2O_4]^+$ $(M+H)^+$, 434.9807; found, 434.9811.



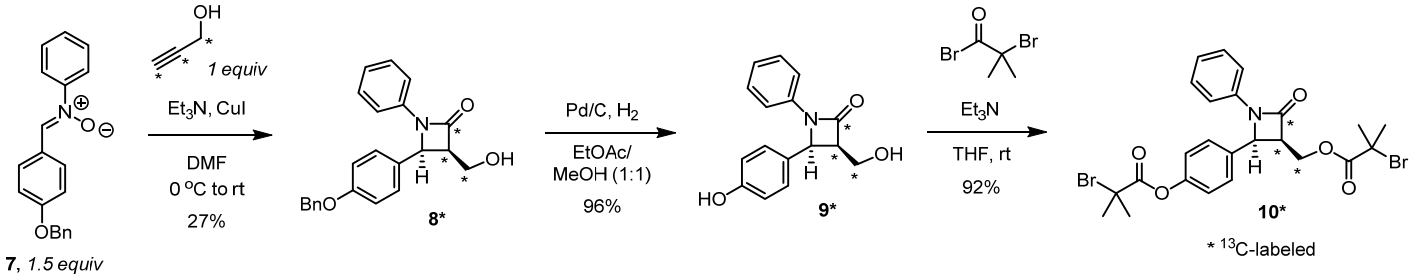
***cis*-4-(4-(pivaloxy)phenyl)-3-pivaloxymethyl-1-phenylazetidin-2-one (4)**. β-Lactam **9** (73 mg, 270 μmol) was dissolved in dry THF (3 mL) in an oven-dried 10 mL round bottom flask equipped with a stir bar and a septum. Triethylamine (80 μL, 570 μmol) was added via syringe followed by the dropwise addition of pivaloyl chloride (70 μL, 570 μmol). After stirring at room temperature overnight, the reaction mixture was filtered through a pad of silica gel, washing thoroughly with ethyl acetate. The filtrate was concentrated under reduced pressure and the crude product was purified by column chromatography (7–50% EtOAC/hexanes) to provide the title compound as a white solid (47 mg, 40%). R_f = 0.57 (EtOAc:hexane 3:7). ^{1}H NMR (500 MHz, Acetone-d_6) δ: 1.07 (s, 9H), 1.32 (s, 9H), 3.92–4.01 (m, 1H), 4.07–4.17 (m, 2H), 5.55 (d, *J* = 5.5 Hz, 1H), 7.04–7.11 (m, 1H), 7.13–7.19 (m, 2H), 7.27–7.35 (m, 4H), 7.42–7.49 (m, 2H) ppm. ^{13}C{^{1}H} NMR (125 MHz, Acetone-d_6) δ: 27.4, 27.5, 39.2, 39.7, 54.7, 57.6, 59.7, 117.9, 123.0, 124.7, 129.3, 130.1, 132.9, 138.9, 152.3, 164.7, 177.0, 177.9 ppm. HRMS (ESI, *m*/*z*): calcd for $[C_{26}H_{32}NO_5]^+$ $(M+H)^+$, 438.2280; found, 438.2283.



Isobutyl 3-acetoxypropionate (5). A 50 mL round bottom flask equipped with a stir bar was charged with 3-acetoxypropanoic acid[4] (590 mg, 4.5 mmol), 2-methyl-1-propanol (500 μL, 5.4 mmol), DMAP (54 mg, 440 μmol), and DCM (15 mL) and sealed with a septum. DCC (1.0 g, 4.8 mmol) was dissolved in DCM (5 mL) and added to the above solution slowly at room temperature. After stirring overnight, the reaction mixture was filtered through a pad of celite and silica gel, washing thoroughly with DCM. The filtrate was concentrated under reduced pressure and the crude product was purified by column chromatography (0–25% EtOAC/hexanes) to provide the title compound as a colorless liquid (740 mg, 88%). R_f = 0.67 (EtOAc:hexane 3:7). ^{1}H NMR (500 MHz, Acetone-d_6) δ: 0.92 (d, *J* = 6.7 Hz, 6H), 1.85–1.97 (m, 1H), 1.97 (s, 3H), 2.67 (t, *J* = 6.2 Hz, 2H), 3.87 (d, *J* = 6.6 Hz, 2H), 4.28 (t, *J* = 6.3 Hz, 2H) ppm. ^{13}C{^{1}H} NMR (125 MHz, Acetone-d_6) δ: 19.4, 20.8, 28.7, 34.5, 60.8, 71.1, 170.9, 171.3 ppm. HRMS (ESI, *m*/*z*): calcd for $[C_9H_{16}O_4Na]^+$ $(M+Na)^+$, 211.0946; found, 211.0952.



(E)-*N*-Phenyl-4-acetoxybenzylideneimine (6). Aniline (970 μL, 10.6 mmol) and 4-acetoxybenzaldehyde (1.50 mL, 10.7 mmol) were combined with toluene (150 mL) in a round bottom flask and the toluene was subsequently removed under reduced pressure (40–50 °C). The crude yellow oil was purified by recrystallization from isopropanol to provide the title compound as a white, shimmery solid (1.65 g, 65%). ^{1}H NMR (500 MHz, Acetone-d_6) δ: 2.30 (s, 3H), 7.21–7.31 (m, 5H), 7.37–7.45 (m, 2H), 7.98–8.05 (m, 2H), 8.59 (s, 1H) ppm. ^{13}C{^{1}H} NMR (125 MHz, Acetone-d_6) δ: 21.1, 121.9, 123.2, 126.9, 130.1, 130.8, 135.1, 153.0, 154.4, 160.1, 169.6 ppm. HRMS (EI, *m*/*z*): calcd for $[C_{15}H_{13}NO_2]^+$ (M^+), 239.0946; found, 239.0948.

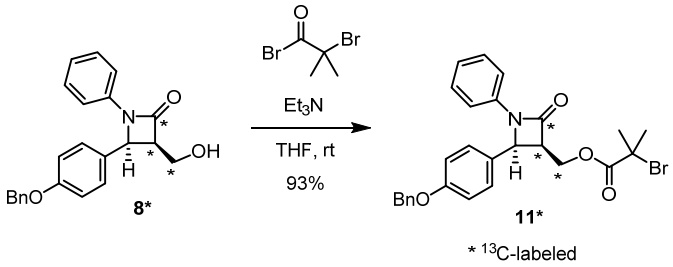


cis*-4-(4-Benzyloxyphenyl)-3-hydroxymethyl-1-phenylazetidin-2-one, ^{13}C-labeled (8*)**. In an analogous manner to **8**, β-lactam **8 was prepared using $^{13}C_3$-labeled propargyl alcohol (150 μL, 2.45 mmol), nitrone **7** (1.11 g, 3.65 mmol), CuI (473 mg, 2.48 mmol), triethylamine (380 μL, 2.73 mmol), and DMF (16 mL). The crude product was purified by column chromatography (30–80% EtOAC/hexanes) to provide the title compound as an off-white solid (237 mg, 27%). ^{1}H NMR (500 MHz, Acetone-d_6) δ: 3.24–4.05 (m, 4H), 5.10 (s, 2H), 5.38 (dt, *J* = 5.9, 3.1 Hz, 1H), 7.01–7.06 (m, 3H), 7.24–7.31 (m, 6H), 7.31–7.36 (m, 1H), 7.37–7.43 (m, 2H), 7.46–7.52 (m, 2H) ppm. ^{13}C{^{1}H} NMR (150 MHz, Acetone-d_6) δ: 57.80 (dd, *J* = 40.8, 1.0 Hz), 58.38 (dd, *J* = 40.6, 39.3 Hz), 70.57 , 115.61 , 117.80 (d, *J* = 2.3 Hz), 124.24 , 128.09 , 128.63 , 128.77 , 129.37 , 129.50 , 129.86 , 138.32 , 139.08 (d, *J* = 5.6 Hz), 159.72, 166.43 (dd, *J* = 38.9, 1.2 Hz) ppm. HRMS (ESI, *m*/*z*): calcd for $[C_{20}{}^{13}C_3H_{22}NO_3]^+$ $(M+H)^+$, 363.1700; found, 363.1695.

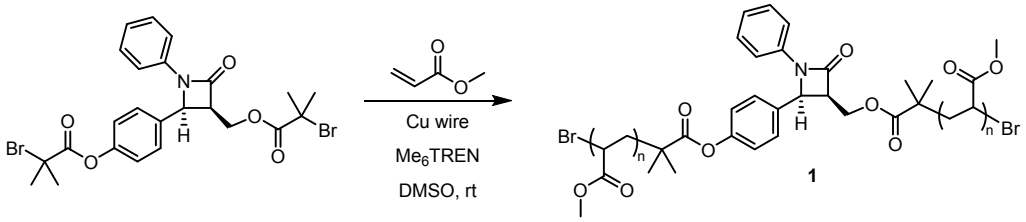
cis*-4-(4-Hydroxyphenyl)-3-hydroxymethyl-1-phenylazetidin-2-one, ^{13}C-labeled (9*)**. Benzyl deprotection was carried out in an identical fashion to the unlabeled compound using **8 (122 mg, 337 μmol), 10% Pd/C (24 mg), ethyl acetate (3 mL) and methanol (3 mL) to provide the title compound as an off-white solid (88 mg, 96%). ^{1}H NMR (500 MHz, Acetone-d_6) δ: 3.21–4.08 (m, 4H), 5.34 (dt, *J* = 5.5, 2.8 Hz, 1H), 6.78–6.89 (m, 2H), 7.03 (tt, *J* = 6.5, 2.1 Hz, 1H), 7.13–7.23 (m, 2H), 7.22–7.37 (m, 4H), 8.46 (s, 1H) ppm. ^{13}C{^{1}H} NMR (150 MHz, Acetone-d_6) δ:

57.76 (dd, *J* = 40.9, 2.6 Hz), 58.26 (dd, *J* = 40.8, 38.0 Hz), 116.19 , 117.73 (d, *J* = 2.3 Hz), 124.12 , 126.45 , 129.38 , 129.75 , 139.05 (d, *J* = 5.4 Hz), 158.13 , 166.48 (dd, *J* = 38.0, 2.6 Hz) ppm. HRMS (ESI, *m*/*z*): calcd for $[C_{13}{}^{13}C_3H_{16}NO_3]^+$ $(M+H)^+$, 273.1231; found, 273.1237.

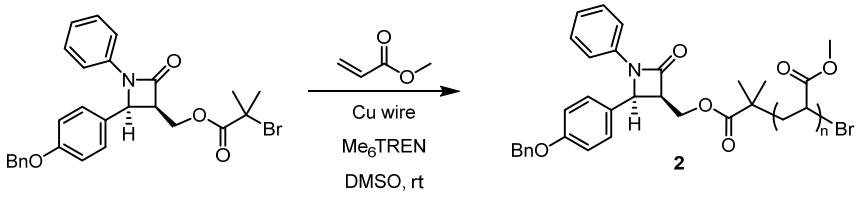
cis*-4-(4-(2-bromoisobutyroxy)phenyl)-3-(2-bromoisobutyroxy)methyl-1-phenylazetidin-2-one, ^{13}C-labeled (10*)**. Using an identical procedure for the unlabeled compound, **9 (57 mg, 209 μmol), triethylamine (70 μL, 500 μmol), and α-bromoisobutyryl bromide (60 μL, 490 μmol) in THF (2 mL) were reacted to provide the title compound as a white solid (110 mg, 92%). ^{1}H NMR (500 MHz, Benzene-d_6) δ: 1.63 (s, 3H), 1.70 (s, 3H), 1.72 (s, 6H), 3.39 (ddp, *J* = 142, 9.3, 5.7 Hz, 1H), 3.79 (dddt, *J* = 150, 12.1, 9.3, 3.0 Hz, 1H), 4.16 (ddtd, *J* = 150, 11.8, 4.4, 2.3 Hz, 1H), 4.35 (dt, *J* = 6.1, 3.2 Hz, 1H), 6.79–6.91 (m, 5H), 6.96–7.03 (m, 2H), 7.31–7.37 (m, 2H) ppm. ^{13}C{^{1}H} NMR (150 MHz, Benzene-d_6) δ: 30.36 , 30.37 , 30.63 , 30.69 , 53.65 (t, *J* = 41.7 Hz), 55.66 , 55.78 , 56.65 (dd, *J* = 30.1, 4.5 Hz), 60.35 (d, *J* = 42.0 Hz), 117.24 (d, *J* = 2.3 Hz), 121.77 , 124.16 , 128.41 , 129.42 , 132.01 , 138.10 (d, *J* = 6.1 Hz), 151.12 , 162.81 (d, *J* = 41.5 Hz), 169.74 , 170.58 ppm. HRMS (ESI, m/z): calcd for $[C_{21}{}^{13}C_3H_{26}Br_2NO_5]^+$ $(M+H)^+$, 569.0278; found, 569.0283.



cis*-4-(4-Benzyloxyphenyl)-3-(2-bromoisobutyroxy)methyl-1-phenylazetidin-2-one, ^{13}C-labeled (11*)**. Using an identical procedure for the unlabeled compound, **8 (61 mg, 168 μmol), triethylamine (35 μL, 250 μmol), and α-bromoisobutyryl bromide (30 μL, 220 μmol) in THF (2 mL) were reacted to provide the title compound as an off-white solid (80 mg, 93%). ^{1}H NMR (500 MHz, Benzene-d_6) δ: 1.63 (s, 3H), 1.69 (s, 3H), 3.42 (dp, *J* = 141, 9.3, 5.8 Hz, 1H), 3.87 (ddt, *J* = 150, 12.1, 9.1, 3.3 Hz, 1H), 4.22 (dtd, *J* = 150, 11.8, 4.3, 2.4 Hz, 1H), 4.42 (dt, *J* = 6.0, 3.1 Hz, 1H), 4.59 (s, 2H), 6.66–6.74 (m, 2H), 6.77–6.86 (m, 3H), 6.98–7.04 (m, 2H), 7.04–7.09 (m, 1H), 7.09–7.15 (m, 2H), 7.17–7.22 (m, 2H), 7.41–7.47 (m, 2H) ppm. ^{13}C{^{1}H} NMR (150 MHz, Acetone-d_6) δ: 31.08 , 54.38 (t, *J* = 41.9 Hz), 56.94 , 57.59 (dd, *J* = 30.3, 4.4 Hz), 61.31 (d, *J* = 42.5 Hz), 70.63 , 116.02 , 117.97 (d, *J* = 2.3 Hz), 124.65 , 127.31 , 128.59 , 128.81 , 129.42 , 129.52 , 130.00 , 138.29 , 138.87 (d, *J* = 6.2 Hz), 159.98 , 164.31 (d, *J* = 41.4 Hz), 171.36 ppm. HRMS (ESI, *m*/*z*): calcd for $[C_{24}{}^{13}C_3H_{27}BrNO_4]^+$ $(M+H)^+$, 511.1224; found, 511.1221.



General procedure for the synthesis of poly(methyl acrylate) (PMA) containing a chain-centered initiating unit. A representative procedure for the synthesis of polymer **1** is provided. A 10 mL oven-dried Schlenk flask equipped with a stir bar and a PTFE valve was charged with freshly cut copper wire (2 cm length, 20 gauge) and initiator **10** (10.6 mg, 18.7 μmol). The flask was sealed with a septum followed by the addition of DMSO (1.0 mL) and methyl acrylate (2.0 mL, 22.2 mmol) via syringe. The solution was deoxygenated via four freeze-pump-thaw cycles and after the final cycle, the flask was warmed to room temperature and backfilled with nitrogen. Me_6TREN (9.9 μL, 37 μmol) was added using a micro syringe to initiate the polymerization. After stirring at room temperature for 110 minutes, the flask was opened to air and the solution was diluted with DCM. The polymer solution was precipitated into cold methanol (3x) and the isolated material was dried thoroughly under vacuum to provide 1.2 g of polymer (63%).



General procedure for the synthesis of poly(methyl acrylate) (PMA) containing the initiating unit at the chain-end. A representative procedure for the synthesis of polymer **2** is provided. A 10 mL oven-dried Schlenk flask equipped with a stir bar and a PTFE valve was charged with freshly cut copper wire (2 cm length, 20 gauge) and initiator **11** (9.3 mg, 18 μmol). The flask was sealed with a septum followed by the addition of DMSO (1.0 mL) and methyl acrylate (2.0 mL, 22.2 mmol) via syringe. The solution was deoxygenated via four freeze-pump-thaw cycles and after the final cycle, the flask was warmed to room temperature and backfilled with nitrogen. Me_6TREN (9.8 μL, 37 μmol) was added using a micro syringe to initiate the polymerization. After stirring at room temperature for 130 minutes, the flask was opened to air and the solution was diluted with DCM. The polymer solution was precipitated into cold methanol (3x) and the isolated material was dried thoroughly under vacuum to provide 1.3 g of polymer (68%).

XI. Sonication Procedures

General procedure for ultrasonication experiments. An oven-dried Suslick cell was fitted with PTFE septum screw caps and cooled under a stream of dry nitrogen. The cell was charged with isobutanol (trapping agent, anhydrous Aldrich) followed by a solution of the polymer dissolved in dry THF. The cell was placed into the collar of the sonicator and screwed onto the probe. The cell was placed in a cooling bath maintained at -10 °C by a temperature controlled immersion cooler. An argon line equipped with a drying tube was introduced into the cell using a PTFE needle and the solution was sparged continuously beginning 30 minutes prior to sonication and for the duration of the sonication experiment. Pulsed ultrasound (0.5 sec on, 1.0 sec off, 25% amplitude, 8.8 W/cm^2) was then applied to the system. Ultrasonic intensity was calibrated using the method described by Berkowski *et al*.[5]

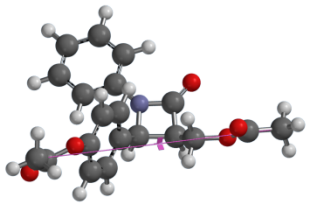
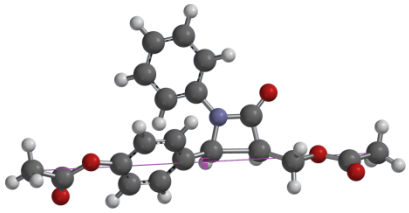
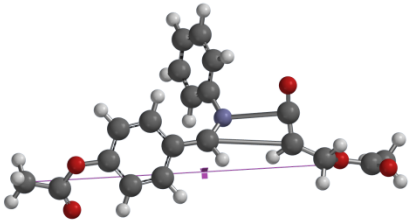
General procedure for ultrasonication experiments for determination of cleavage rate. Each polymer was thoroughly dried under high vacuum and then dissolved in dry THF to afford a stock solution with a concentration of 3.5 mg/mL. The polymer solution (11 mL) and isobutanol (320 μL, ~6,500 equiv) were transferred to the Suslick cell via syringe and sonication was started according to the general procedure above. Aliquots (400–500 μL) were removed at 0, 30, 60, 90, and 120 min (sonication "on" time) and the solvent was removed under a stream of nitrogen. Each sample was subsequently dried under vacuum and redissolved in a volume of THF to afford a 6 mg/mL solution, filtered through a 0.45 μm PTFE syringe filter, and analyzed by GPC.

General procedure for ultrasonication experiments for subsequent analysis by NMR spectroscopy. Each polymer was thoroughly dried under high vacuum and then dissolved in dry THF to afford a solution with a concentration of 5.0–5.4 mg/mL. The polymer solution (11 mL) and isobutanol (680–730 μL, ~10,000 equiv) were transferred to the Suslick cell via syringe and sonication was started according to the general procedure above. After 180 min (sonication "on" time), sonication was stopped and an aliquot (500 μL) was removed for GPC analysis. The remaining solution was concentrated under reduced pressure. The polymer was redissolved in DCM (1 mL) and precipitated into 100 mL of cold methanol (dry ice). The polymer was collected and dried thoroughly under vacuum prior to analysis by NMR spectroscopy.

XII. CoGEF Analysis

CoGEF calculations were performed using Spartan '14 according to previously reported methods.[6–8] Ground state energies were calculated using DFT at the B3LYP 6-31G* level of theory. Starting from the equilibrium geometry of the unconstrained molecule (Energy = 0 kJ/mol), the distance between the methyl esters of the truncated structure was increased in increments of approximately 0.1 Å (~0.05 Å in the region surrounding the breaking point) and the energy was minimized at each interval. Fragmentation of the *cis*-β-lactam ring occurs after the molecule is elongated > 3.917 Å from equilibrium with a relative energy of 284 kJ/mol, generating an imine and a ketene functional group.

Table S1. Structures of the *cis*-β-lactam molecule predicted by density functional calculations (CoGEF) at specific increments of elongation (B3LYP 6-31G*).

Equilibrium Geometry	Immediately Prior to Fragmentation	Immediately After Fragmentation
		
11.467 Å	15.384 Å	15.412 Å

XIII. Determination of Sonication-Induced Rates of Cleavage

Sonication experiments were performed in triplicate for each polymer with each data point representing the average of three runs and the standard deviation of the measurements. Statistical analysis was performed with OriginPro 2015 software. The rate constants of polymer cleavage (k') were calculated from the slope of the least squares linear regression of the data according to the method of Kryger *et al*.[8] using eq 1:

$$\frac{1}{M_t} - \frac{1}{M_i} = k't \tag{1}$$

where M_t is the number average molecular weight (M_n) of the sonicated sample at time t, M_i is the initial number average molecular weight of the polymer, and k' is the rate constant of polymer cleavage adjusted for the molecular weight of the monomer unit, M_0 ($k'=k/M_0$). For simplicity and consistency with previously reported data, the polymer-specific (PMA, $M_0 = 86.1$ Da) rate constants k' were compared.

XIV. References

(1) Davies, S.; Bauer, C.; Barker, P.; Freeman, R. *J. Magn. Reson.* **1985**, *64*, 155–159.

(2) Evans, D. A.; Song, H.-J.; Fandrick, K. R. *Org. Lett.* **2006**, *8*, 3351–3354.

(3) Basak, A.; Bhattacharya, G.; Bdour, H. M. M. *Tetrahedron* **1998**, *54*, 6529–6538.

(4) Catry, M. A.; Madder, A. *Molecules* **2007**, *12*, 114–129.

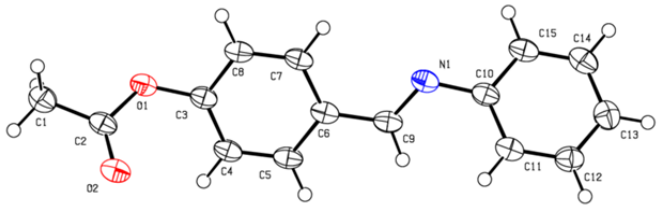
(5) Berkowski, K. L.; Potisek, S. L.; Hickenboth, C. R.; Moore, J. S. *Macromolecules* **2005**, *38*, 8975–8978.

(6) Beyer, M. K. *J. Chem. Phys.* **2000**, *112*, 7307–7312.

(7) Davis, D. A.; Hamilton, A.; Yang, J.; Cremar, L. D.; Van Gough, D.; Potisek, S. L.; Ong, M. T.; Braun, P. V.; Martínez, T. J.; White, S. R.; Moore, J. S.; Sottos, N. R. *Nature* **2009**, *459*, 68–72.

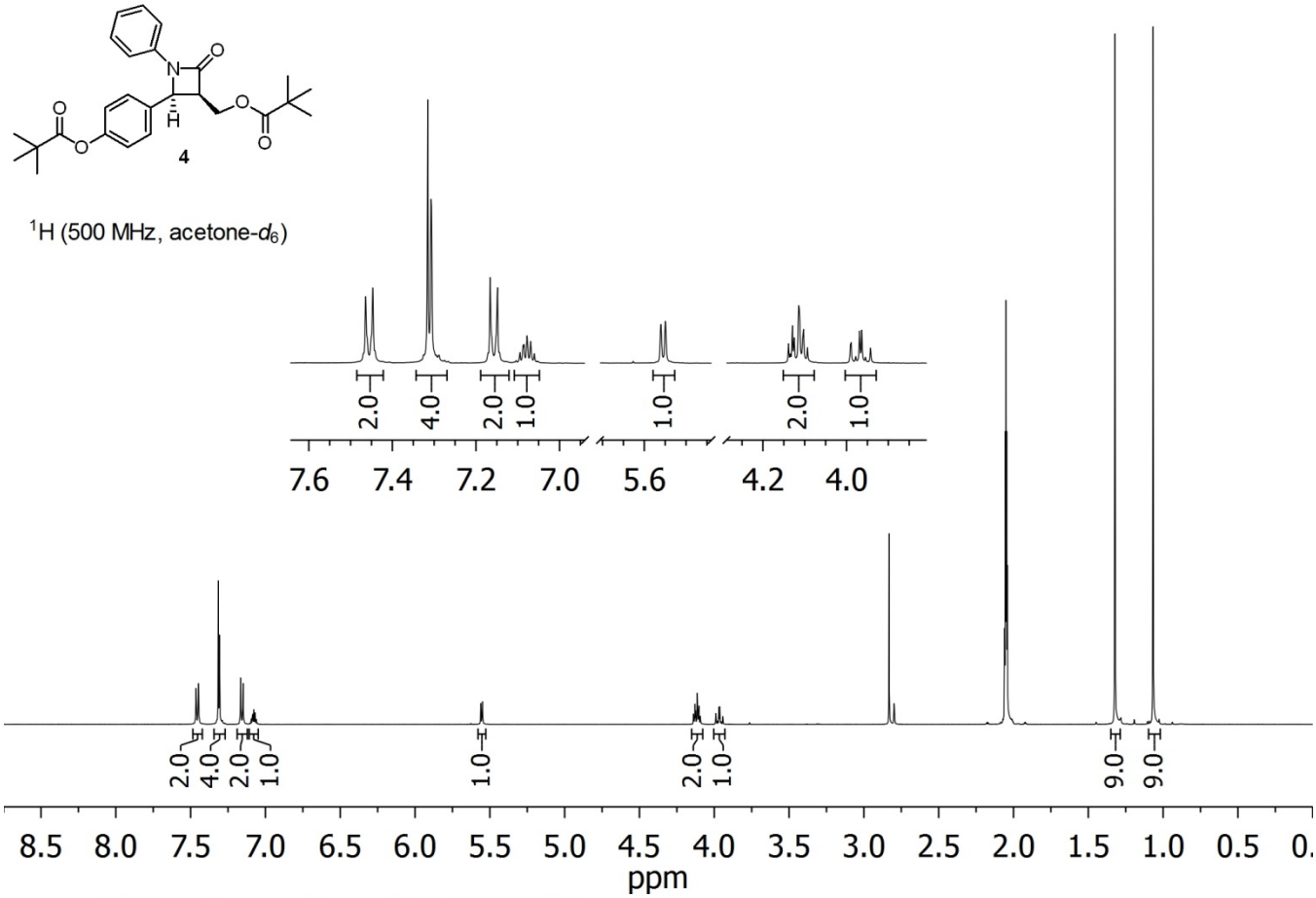
(8) Kryger, M. J.; Munaretto, A. M.; Moore, J. S. *J. Am. Chem. Soc.* **2011**, *133*, 18992–18998.

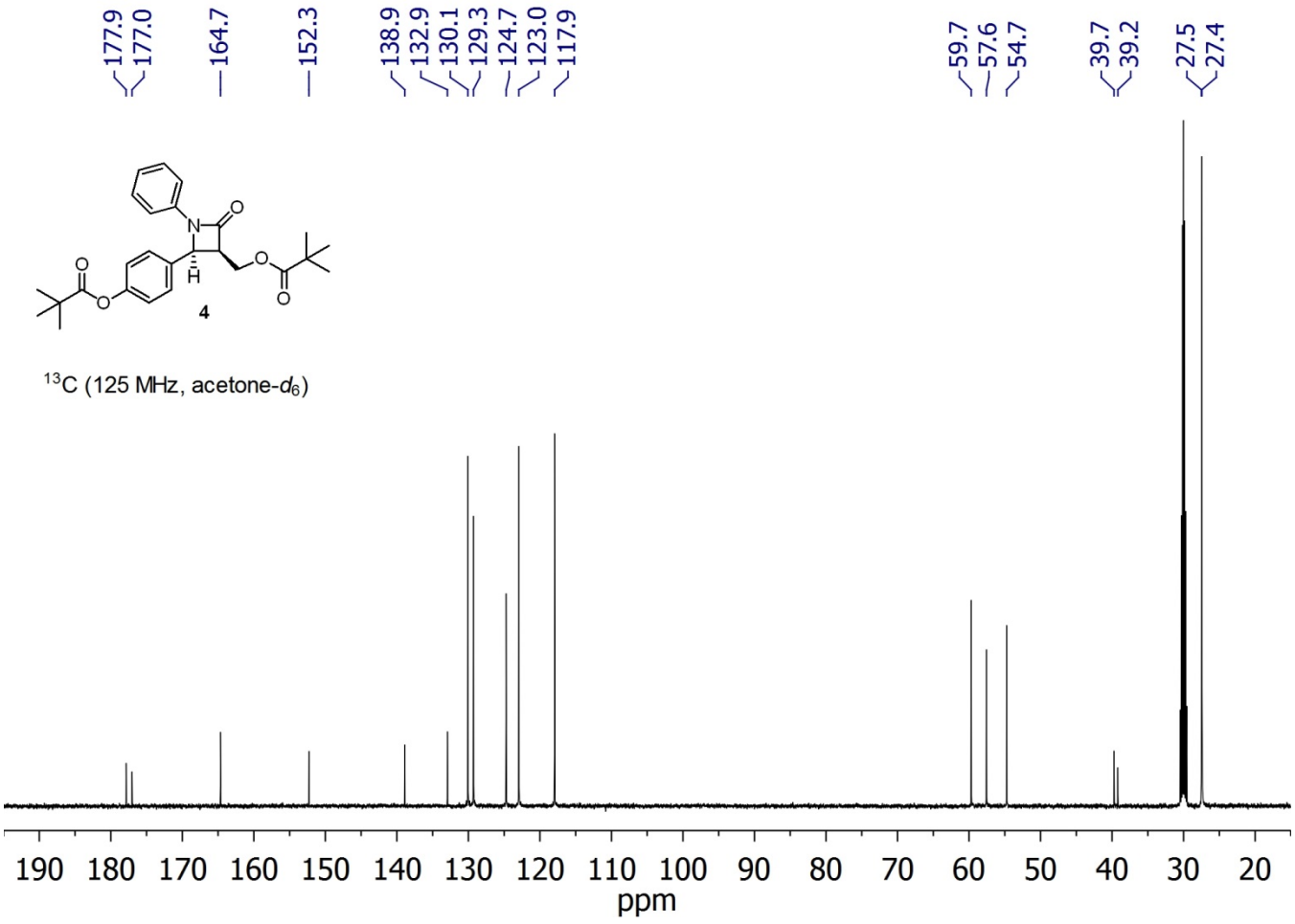
XV. Crystal Structure of Model Compound 6

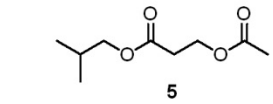


Crystal data and structure refinement for (E)-*N*-Phenyl-4-acetoxybenzylideneimine (6).

Empirical formula	$C_{15}H_{13}NO_2$	
Formula weight	239.26	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions	a = 6.0443(3) Å	α = 90°
	b = 30.6647(15) Å	β = 112.4421(13)°
	c = 7.1534(3) Å	γ = 90°
Volume	1225.45(10) $Å^3$	
Z	4	
Density (calculated)	1.297 g/cm^3	
Absorption coefficient	0.698 mm^{-1}	
F(000)	504	
Crystal size	0.34 x 0.258 x 0.046 mm^3	
Theta range for data collection	2.882 to 68.343°	
Index ranges	$-7 \le h \le 7$	
	$-36 \le k \le 36$	
	$-8 \le l \le 8$	
Reflections collected	23443	
Independent reflections	2227 [R(int) = 0.0495]	
Completeness to theta = 67.679°	99.1 %	
Absorption correction	Integration	
Max. and min. transmission	0.97448 and 0.85956	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2227 / 0 / 165	
Goodness-of-fit on F^2	1.055	
Final R indices [I>2sigma(I)]	R1 = 0.0460, wR2 = 0.1217	
R indices (all data)	R1 = 0.0532, wR2 = 0.1279	
Extinction coefficient	0.0088(9)	
Largest diff. peak and hole	0.245 and -0.246 $e.Å^{-3}$	

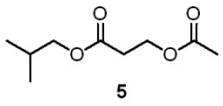

4
^{1}H (500 MHz, acetone-d_6)
2.0
4.0
2.0
1.0
1.0
2.0
1.0
7.6
7.4
7.2
7.0
5.6
4.2
4.0
2.0
4.0
2.0
1.0
1.0
2.0
1.0
9.0
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm


177.9
177.0
164.7
152.3
138.9
132.9
130.1
129.3
124.7
123.0
117.9
59.7
57.6
54.7
39.7
39.2
27.5
27.4
4
^{13}C (125 MHz, acetone-d_6)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm



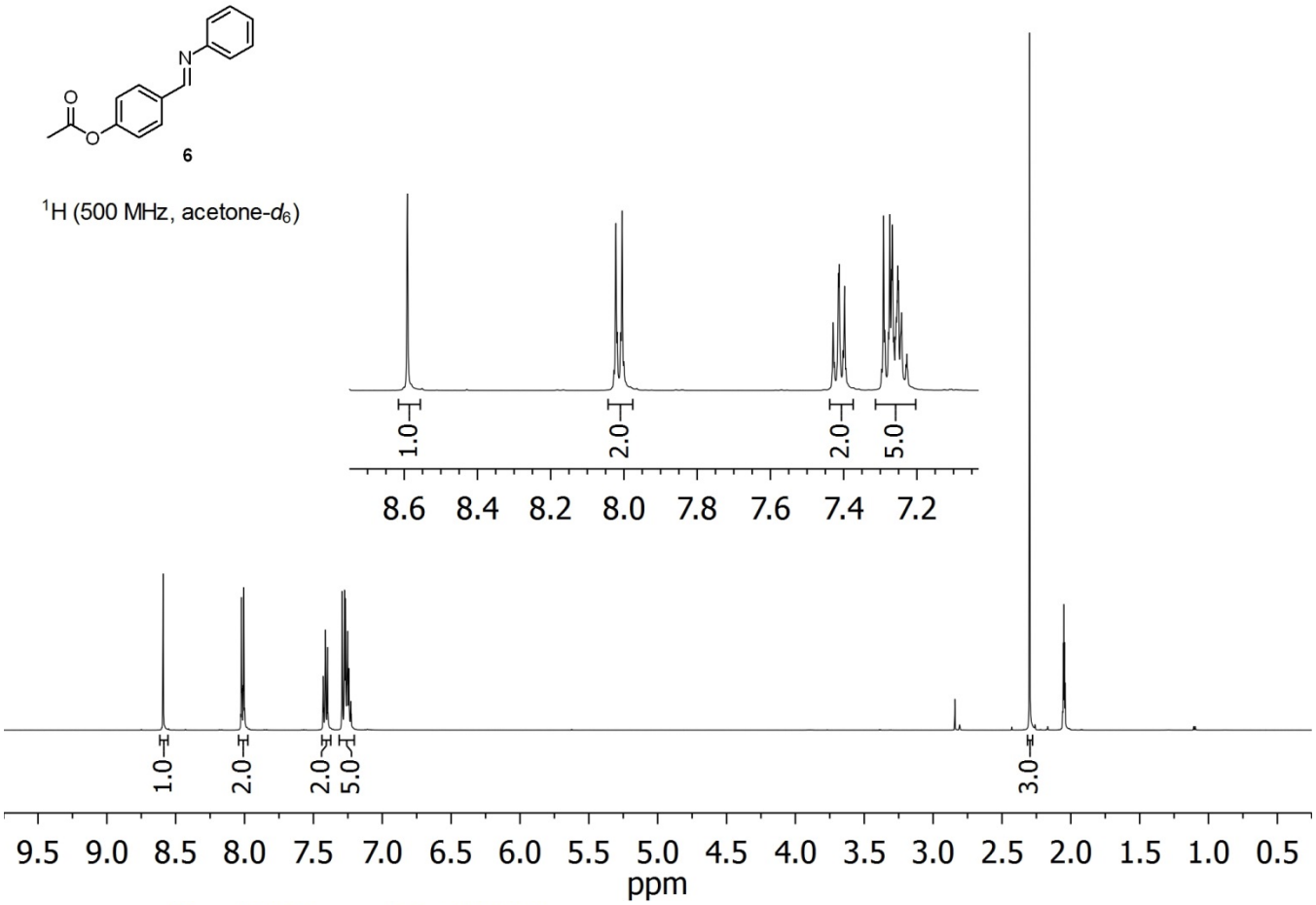
5

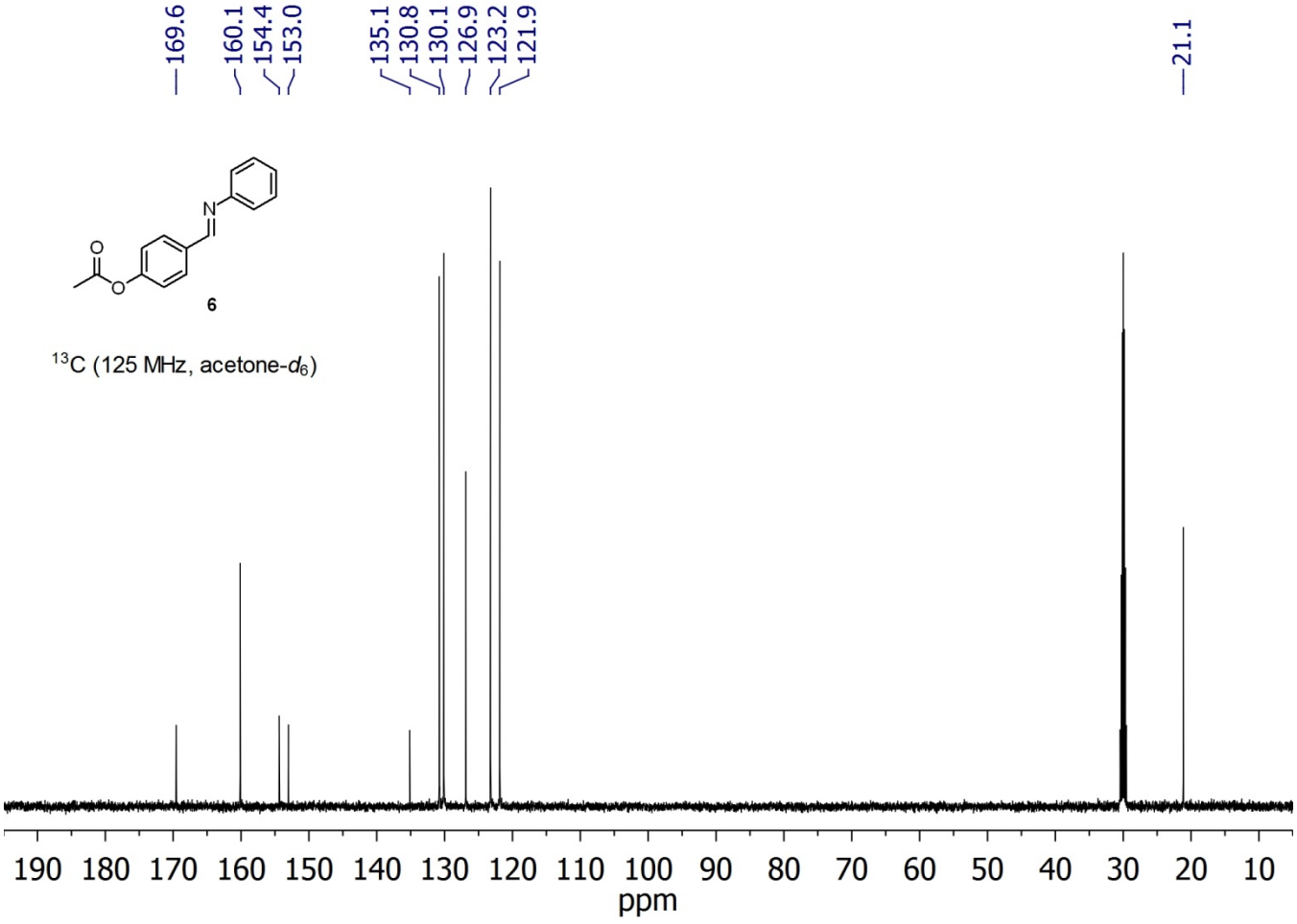
^{1}H (500 MHz, acetone-d_6)

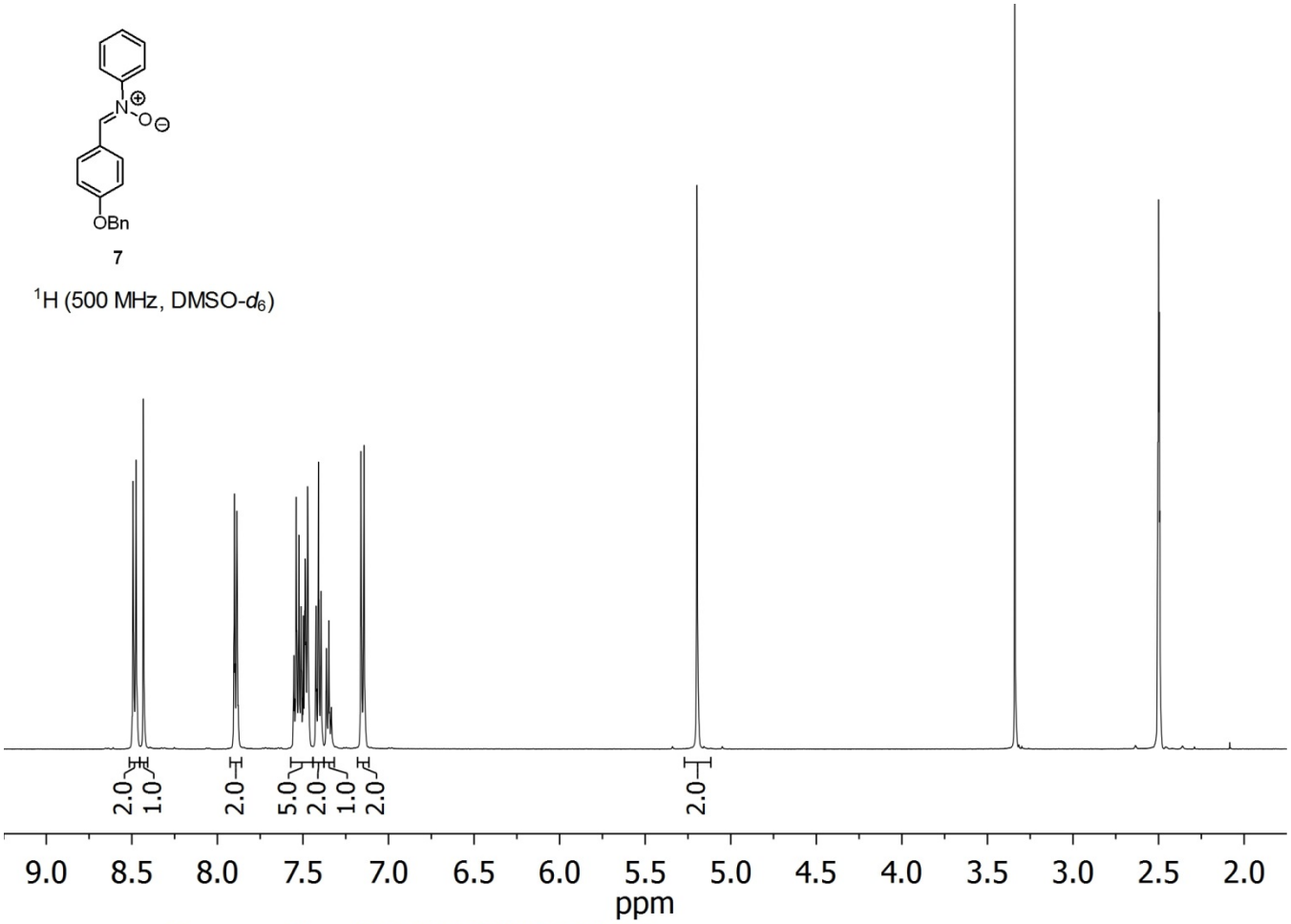


5

^{13}C (125 MHz, acetone-d_6)


6
^{1}H (500 MHz, acetone-d_6)
1.0
2.0
2.0
5.0
3.0
8.6 8.4 8.2 8.0 7.8 7.6 7.4 7.2
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
ppm


169.6
160.1
154.4
153.0
135.1
130.8
130.1
126.9
123.2
121.9
21.1
6
^{13}C (125 MHz, acetone-d_6)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
ppm


OBn
7
^{1}H (500 MHz, DMSO-d_6)
2.0
1.0
2.0
5.0
2.0
1.0
2.0
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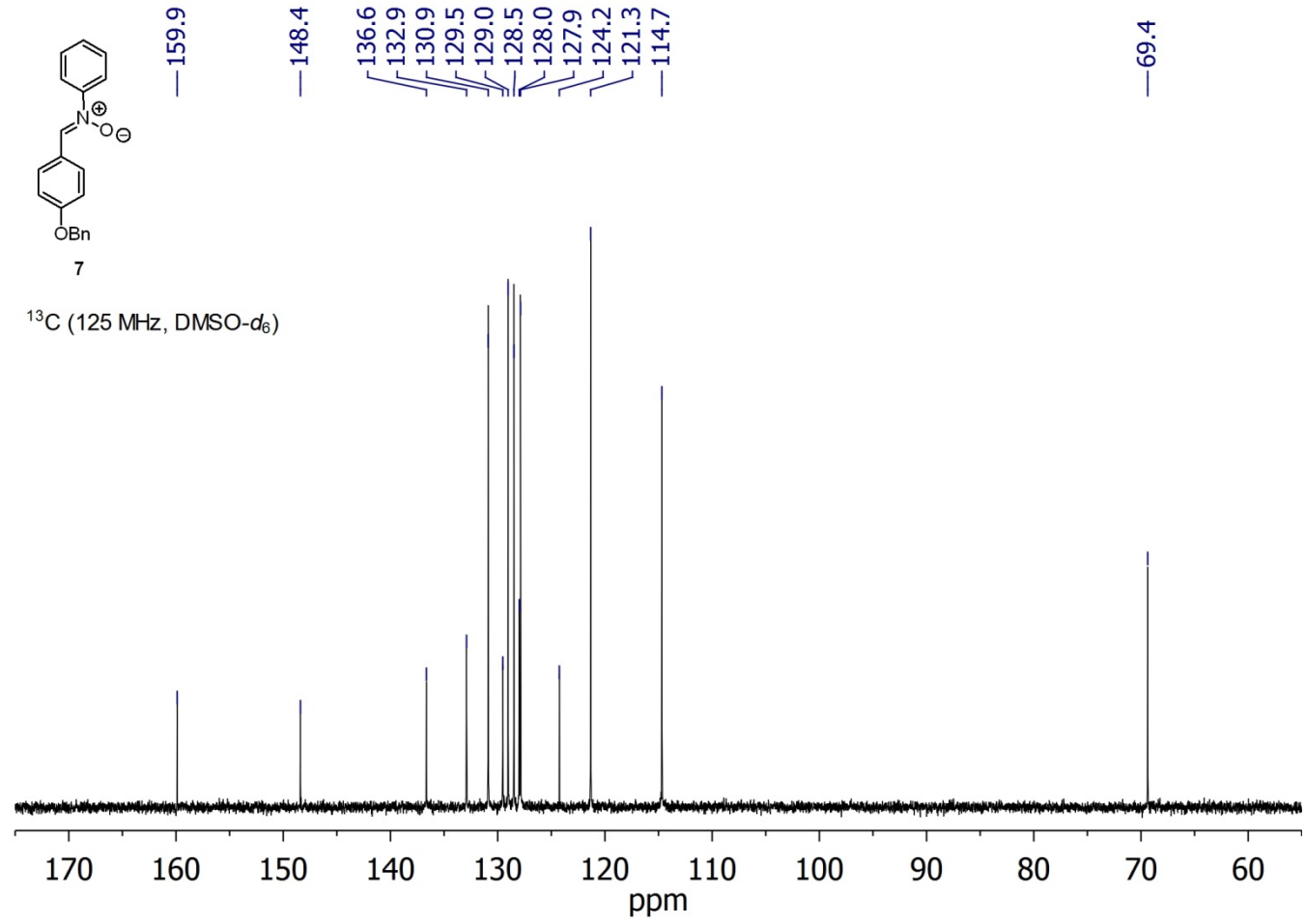
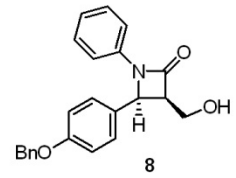
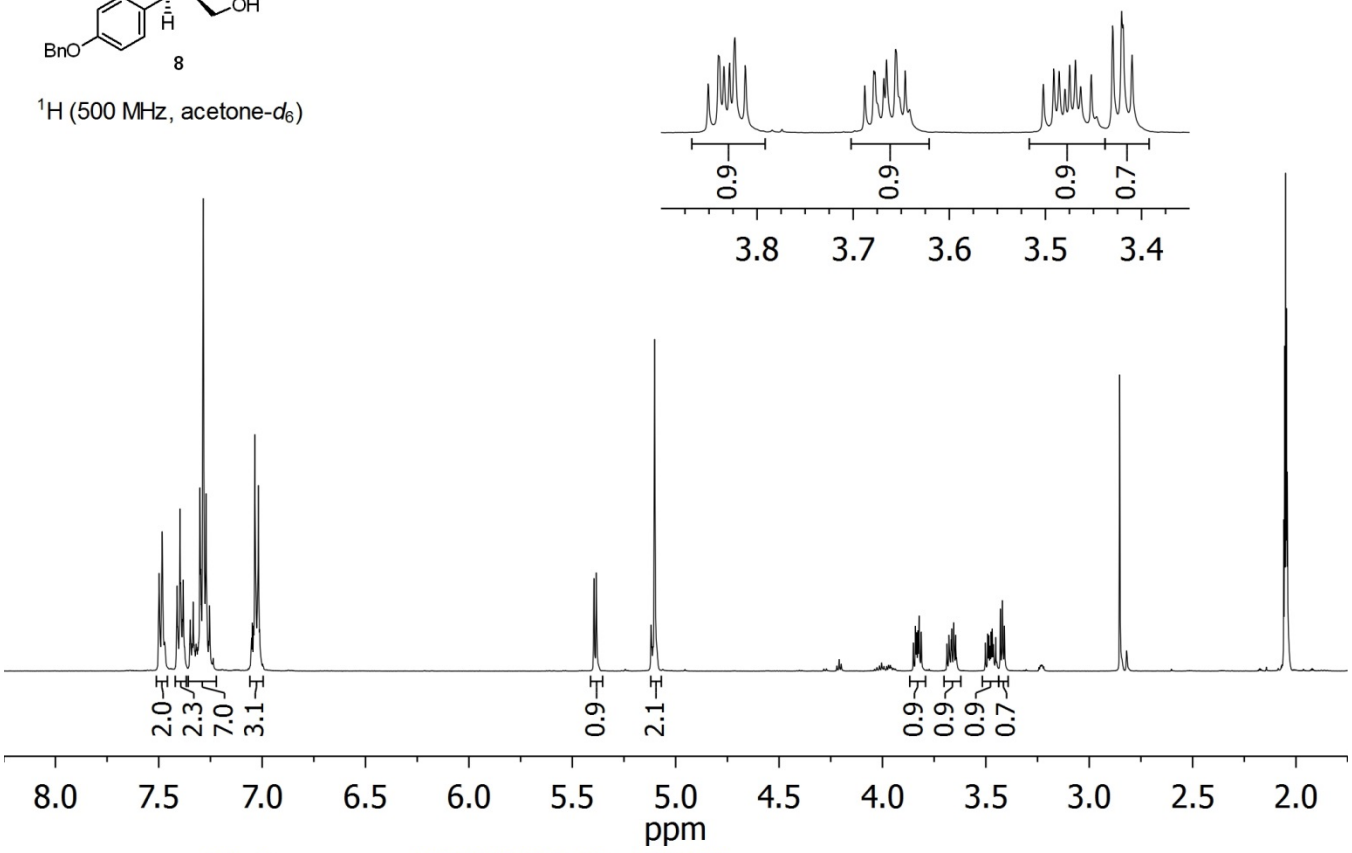
ppm

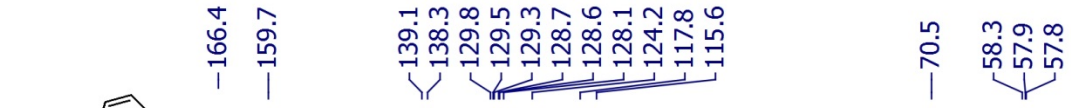

159.9
148.4
136.6
132.9
130.9
129.5
129.0
128.5
128.0
127.9
124.2
121.3
114.7
69.4
OBn
7
^{13}C (125 MHz, DMSO-d_6)
170 160 150 140 130 120 110 100 90 80 70 60
ppm

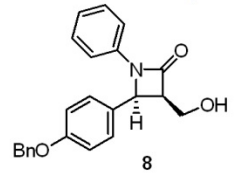


8

^{1}H (500 MHz, acetone-d_6)

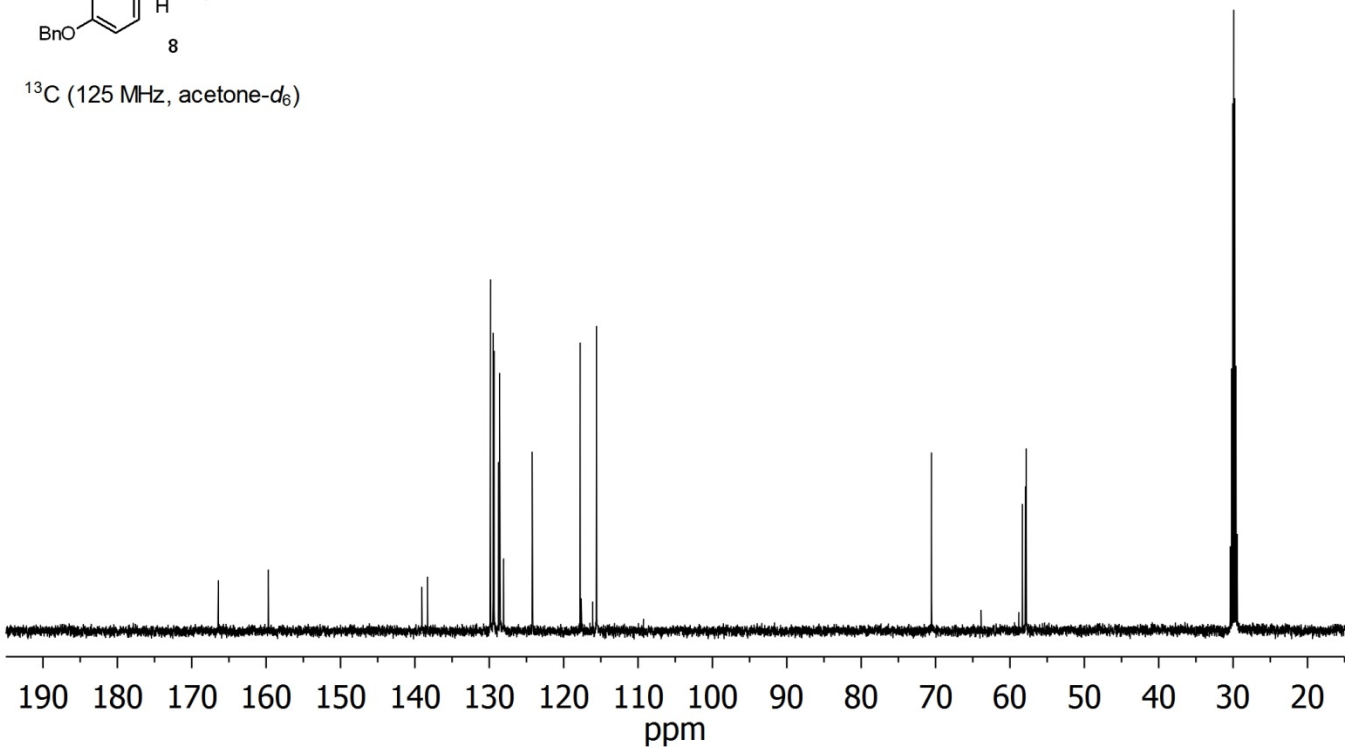


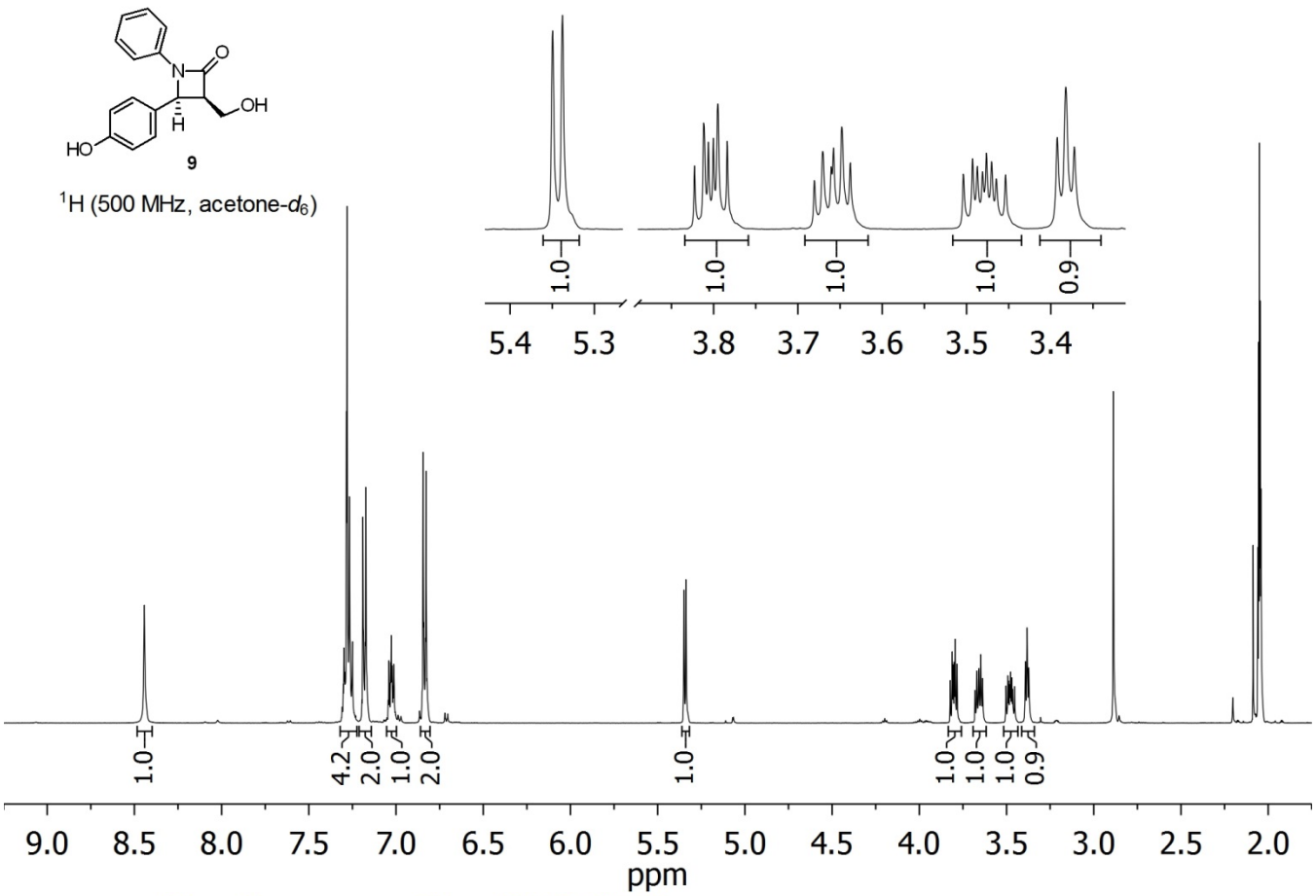


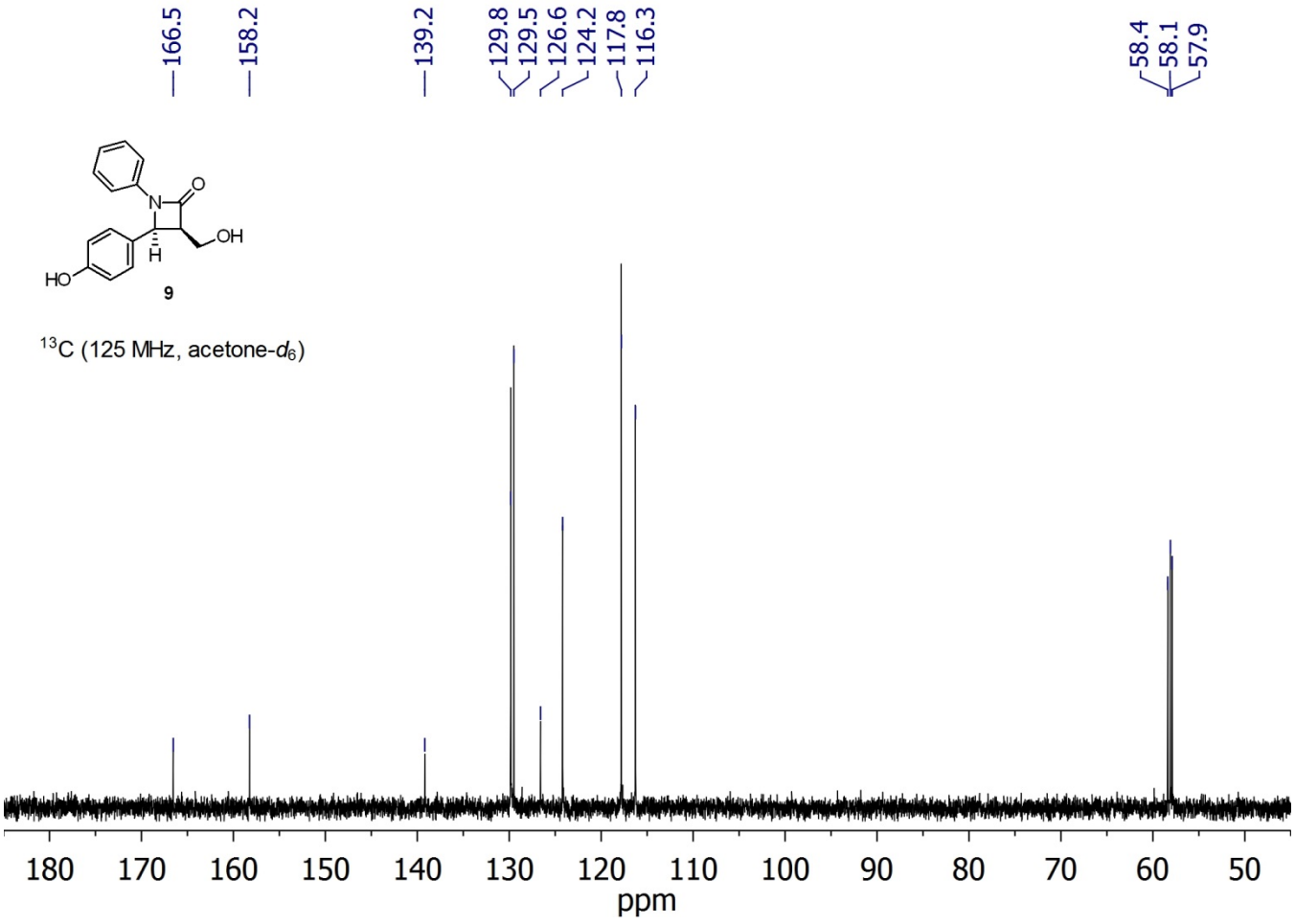


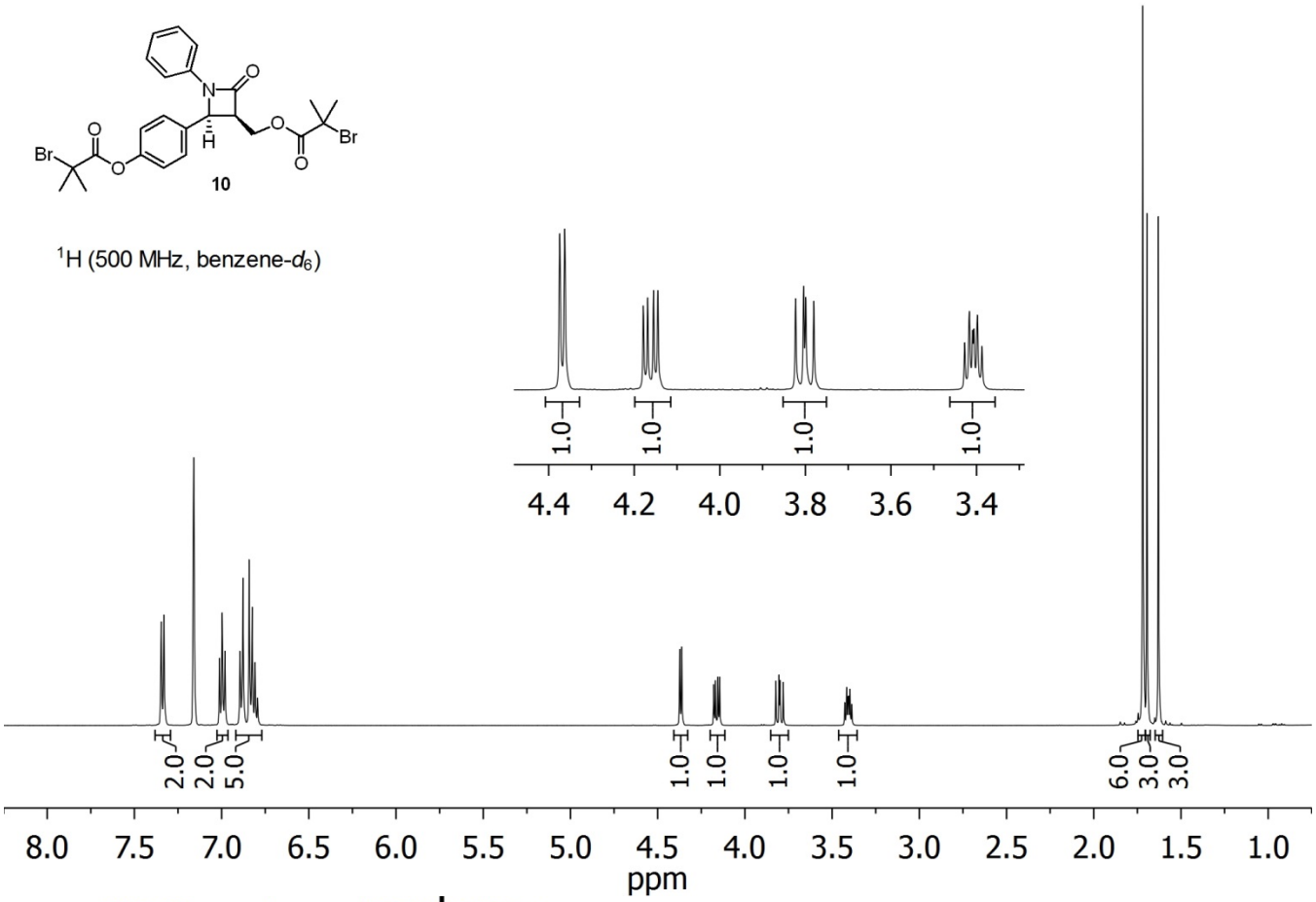
8

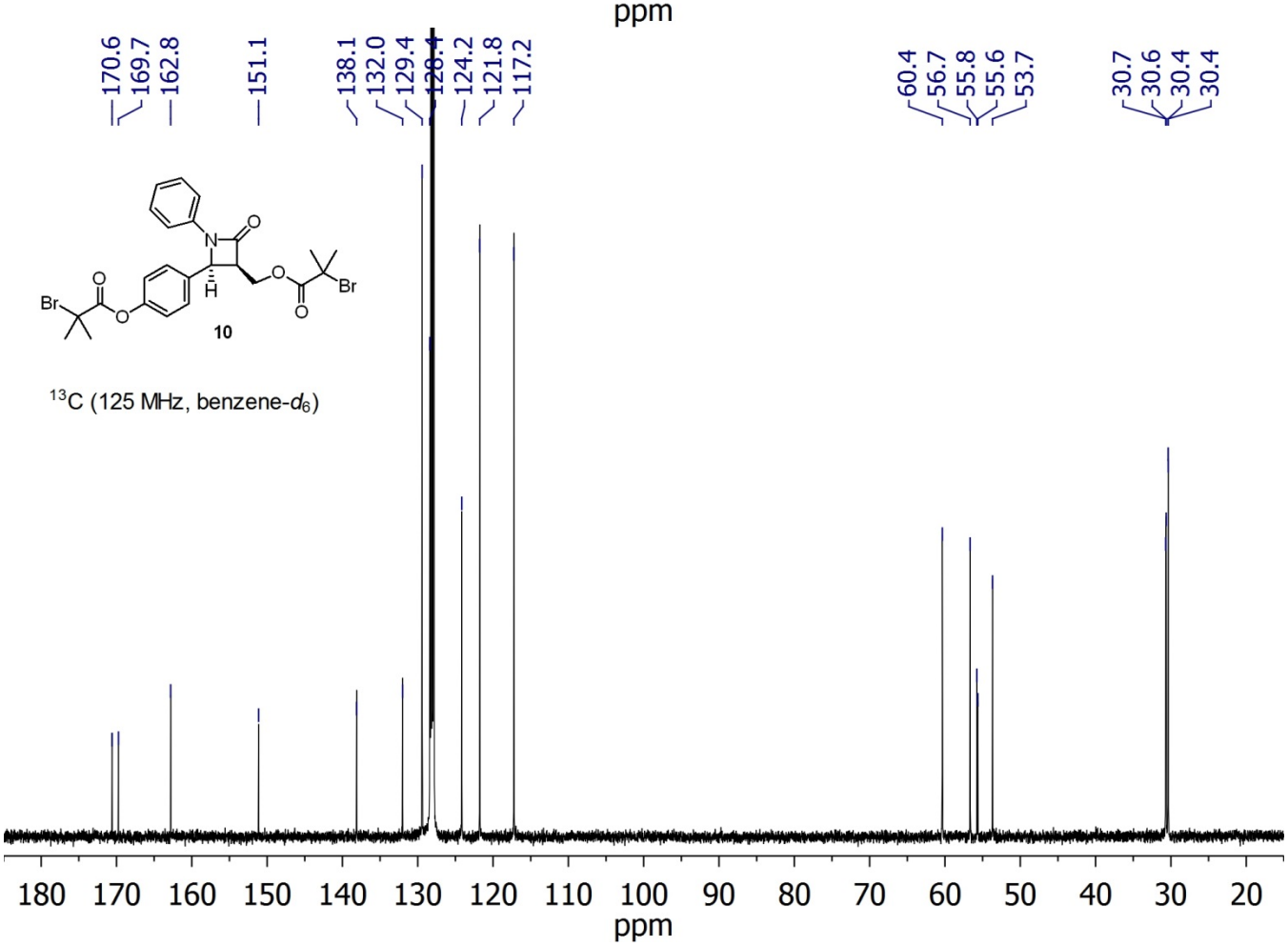
^{13}C (125 MHz, acetone-d_6)

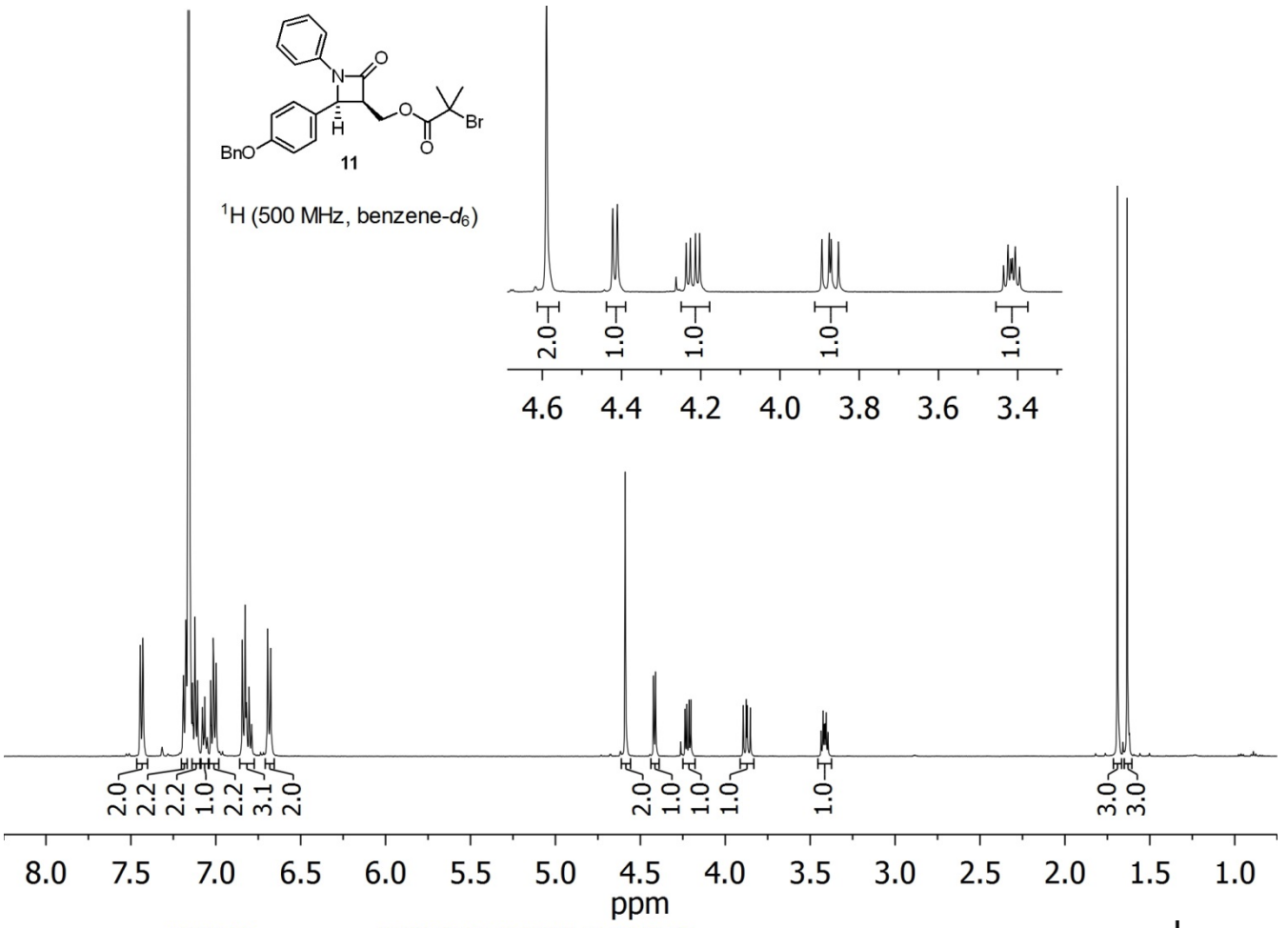


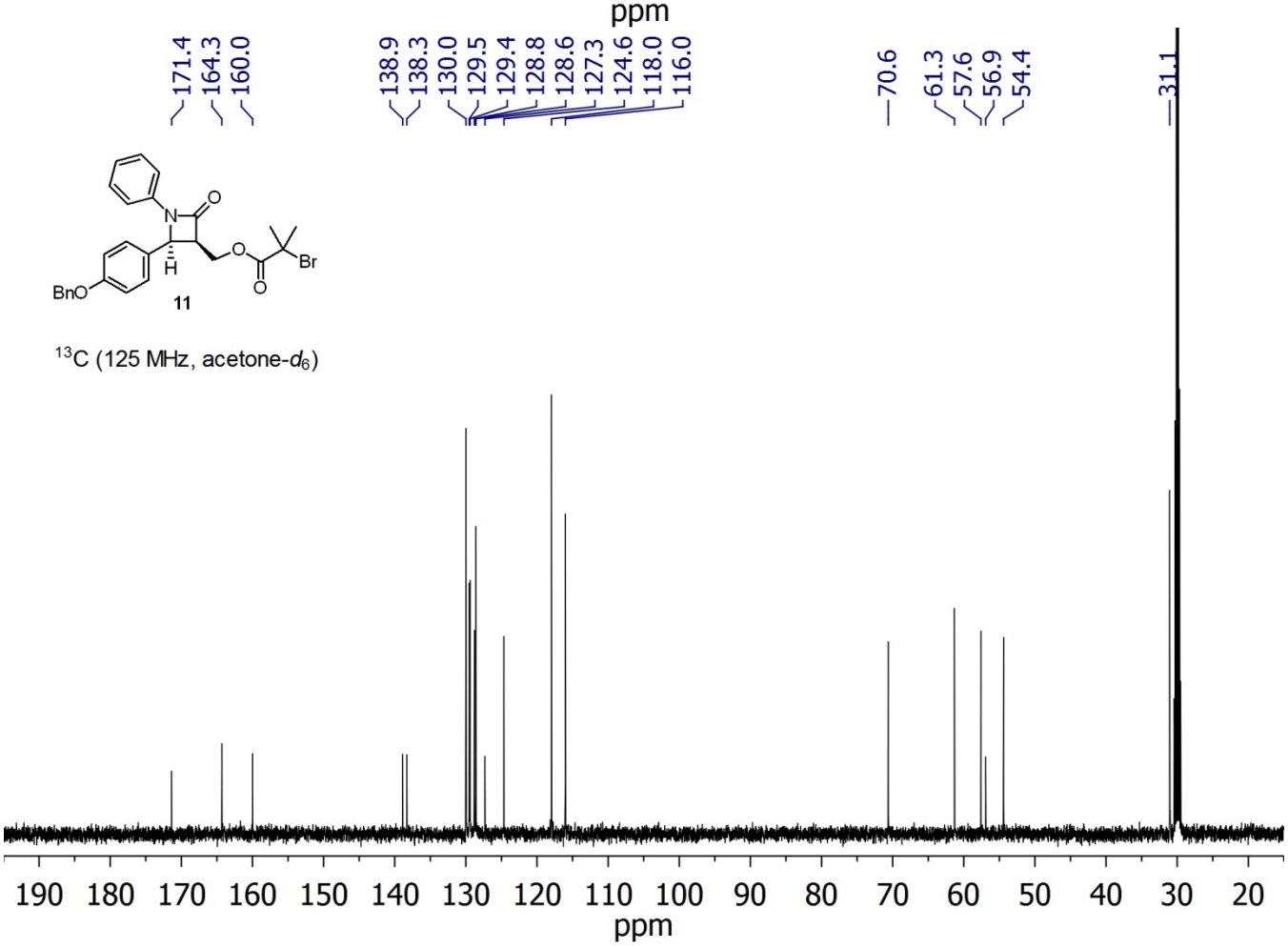

9
^{1}H (500 MHz, acetone-d_6)
1.0
4.2
2.0
1.0
2.0
1.0
1.0
1.0
1.0
0.9
5.4
5.3
3.8
3.7
3.6
3.5
3.4
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
ppm

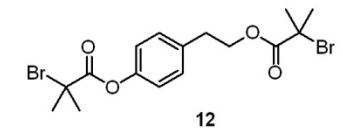

166.5
158.2
139.2
129.8
129.5
126.6
124.2
117.8
116.3
58.4
58.1
57.9
9
^{13}C (125 MHz, acetone-d_6)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
ppm


10
^{1}H (500 MHz, benzene-d_6)
2.0
2.0
5.0
1.0
1.0
1.0
1.0
6.0
3.0
3.0
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
ppm


170.6
169.7
162.8
151.1
138.1
132.0
129.4
128.4
124.2
121.8
117.2
60.4
56.7
55.8
55.6
53.7
30.7
30.6
30.4
30.4
10
^{13}C (125 MHz, benzene-d_6)
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
ppm

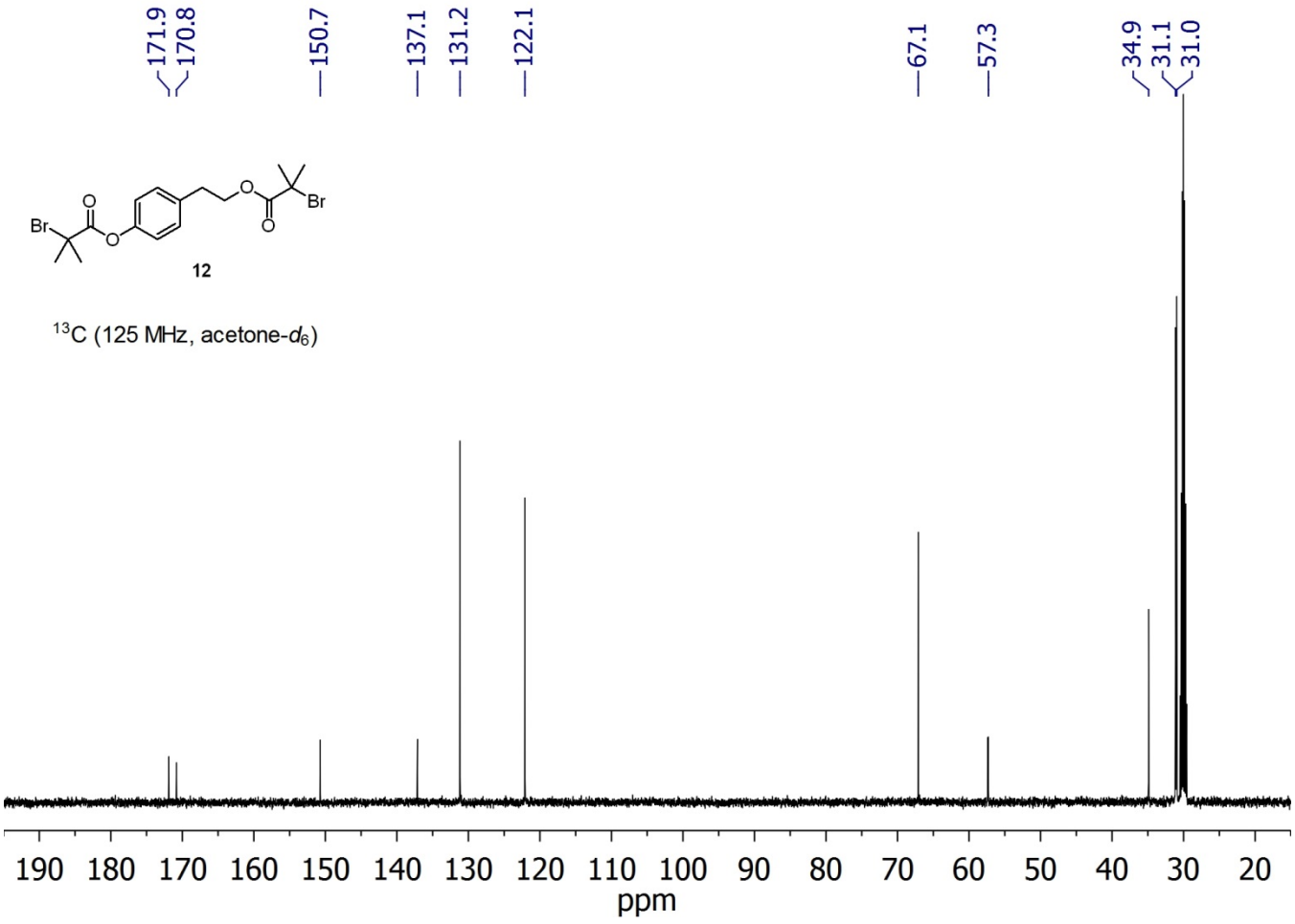

BnO
11
^{1}H (500 MHz, benzene-d_6)
2.0
1.0
1.0
1.0
1.0
4.6
4.4
4.2
4.0
3.8
3.6
3.4
2.0
2.2
2.2
1.0
2.2
3.1
2.0
2.0
1.0
1.0
1.0
1.0
3.0
3.0
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm


171.4
164.3
160.0
138.9
138.3
130.0
129.5
129.4
128.8
128.6
127.3
124.6
118.0
116.0
70.6
61.3
57.6
56.9
54.4
31.1
BnO
11
^{13}C (125 MHz, acetone-d_6)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm



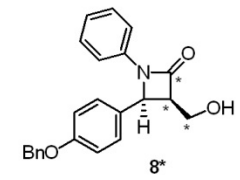
12

^{1}H (500 MHz, acetone-d_6)



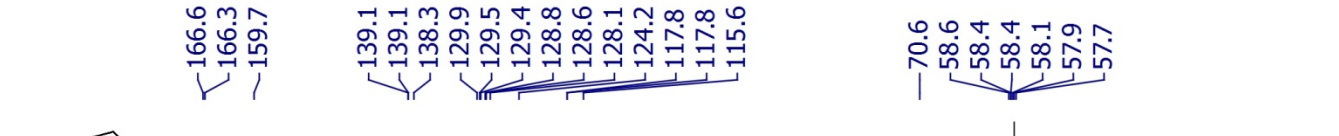
12

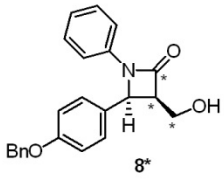
^{13}C (125 MHz, acetone-d_6)



8*

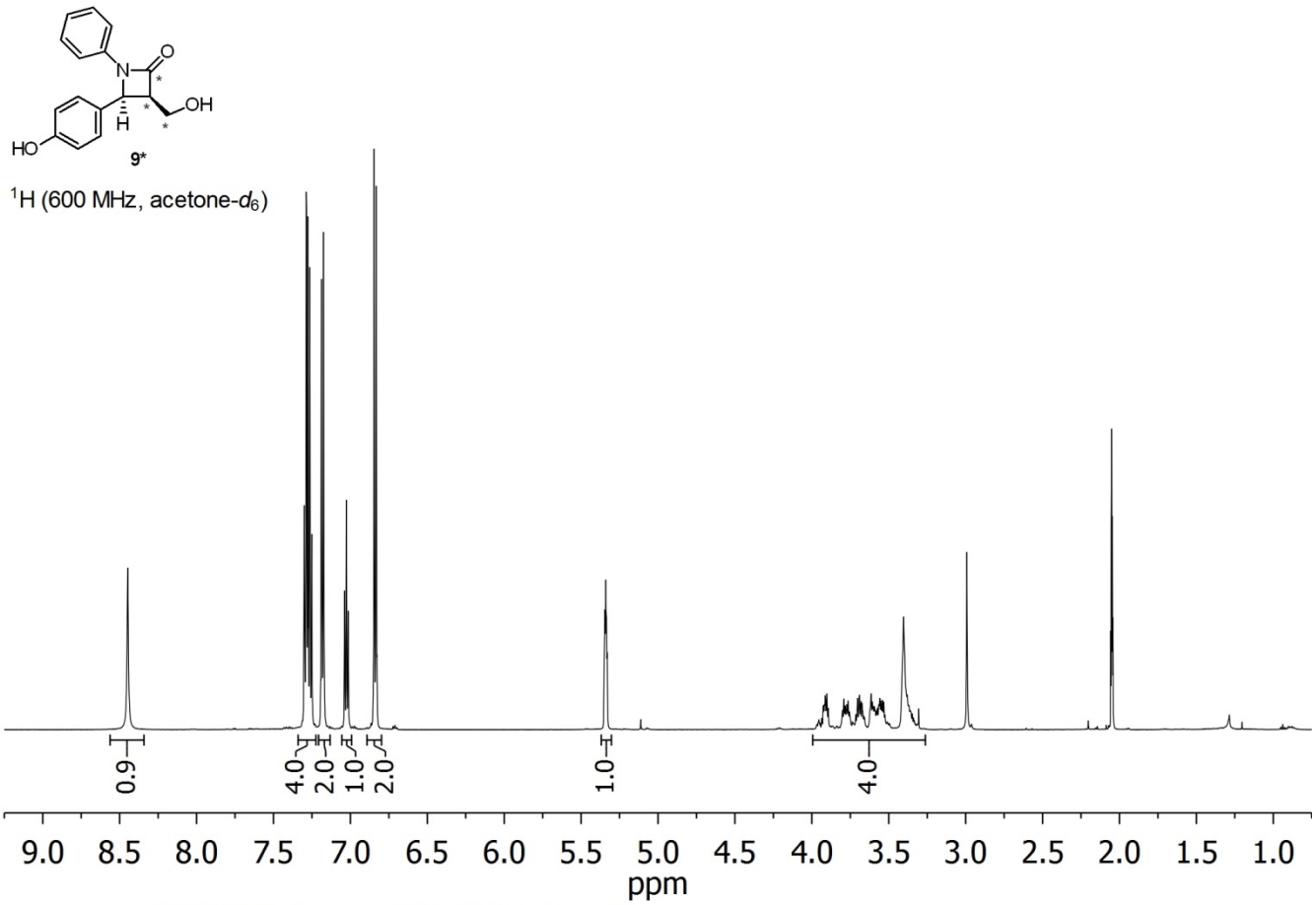
^{1}H (500 MHz, acetone-d_6)

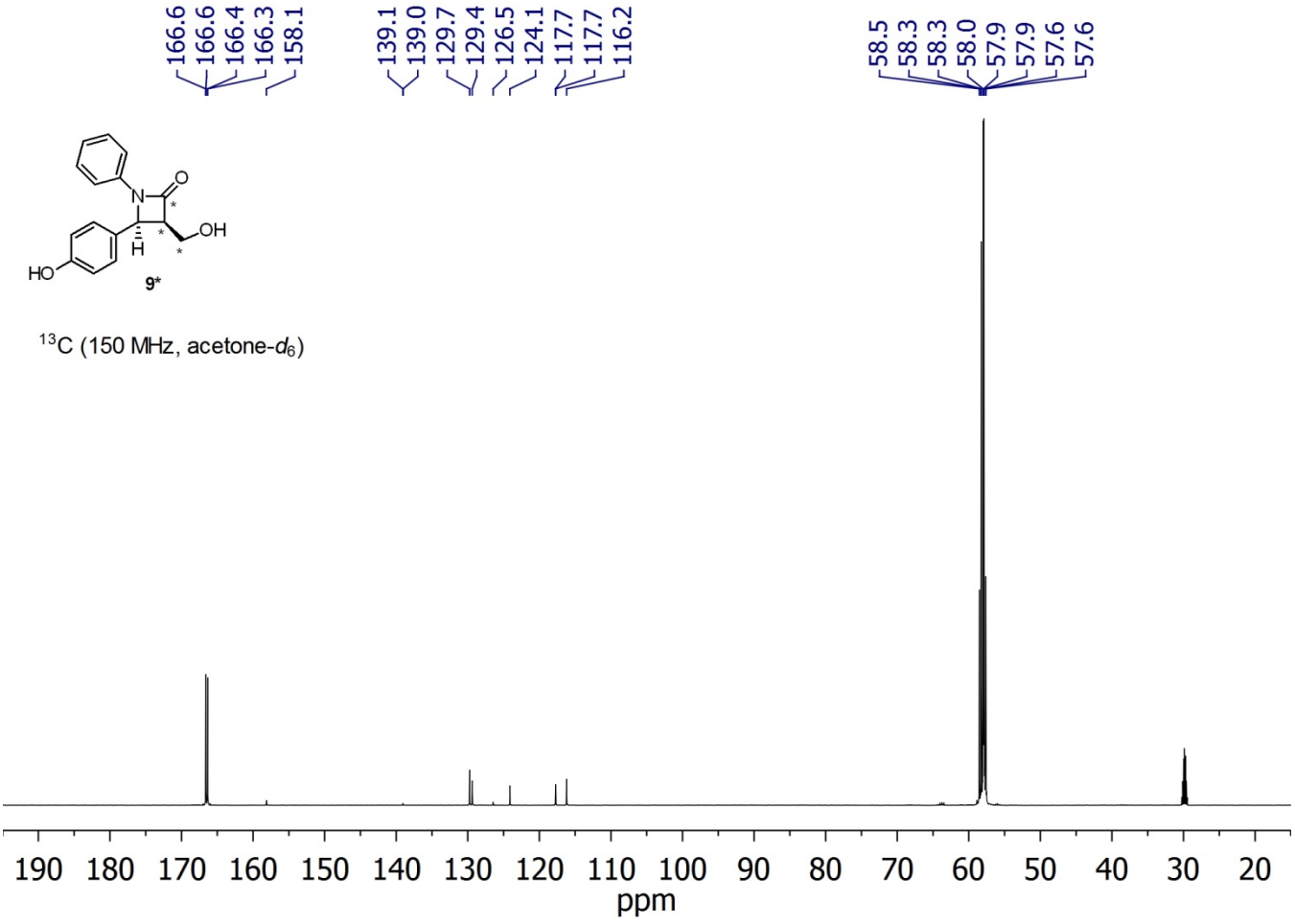


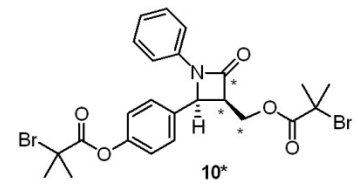


8*

^{13}C (150 MHz, acetone-d_6)

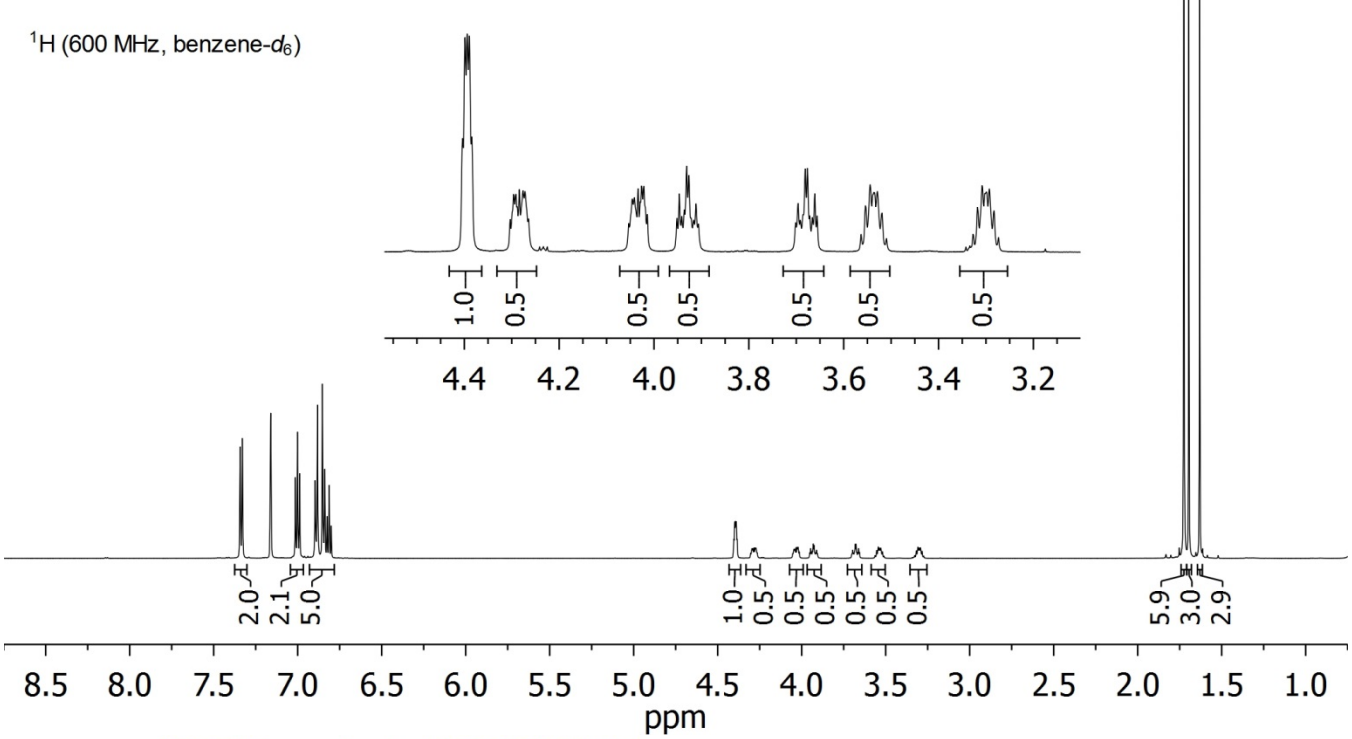

9*
^{1}H (600 MHz, acetone-d_6)
0.9
4.0
2.0
1.0
2.0
1.0
4.0
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
ppm

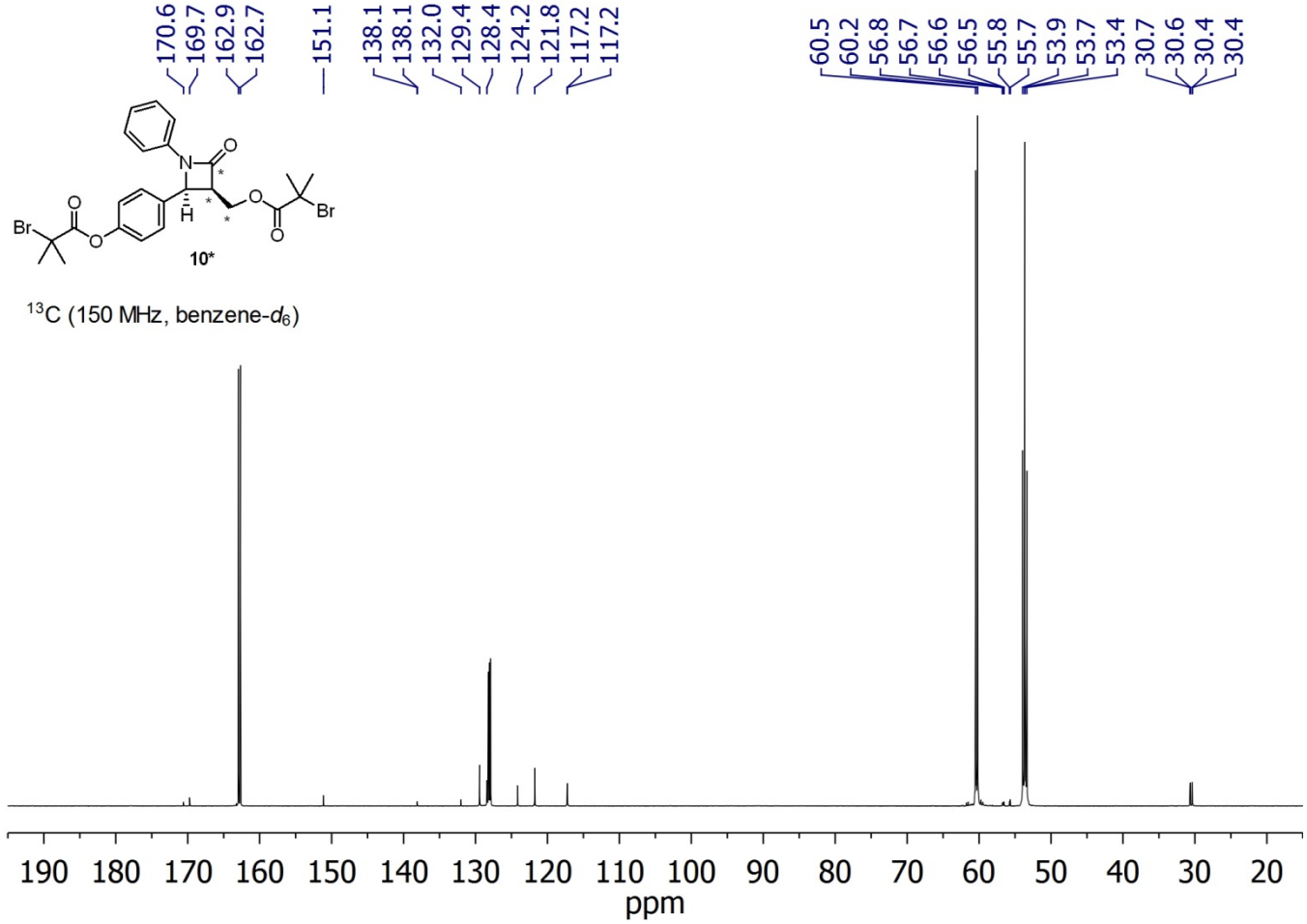

166.6
166.6
166.4
166.3
158.1
139.1
139.0
129.7
129.4
126.5
124.1
117.7
117.7
116.2
58.5
58.3
58.3
58.0
57.9
57.9
57.6
57.6
9*
^{13}C (150 MHz, acetone-d_6)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
ppm



10*

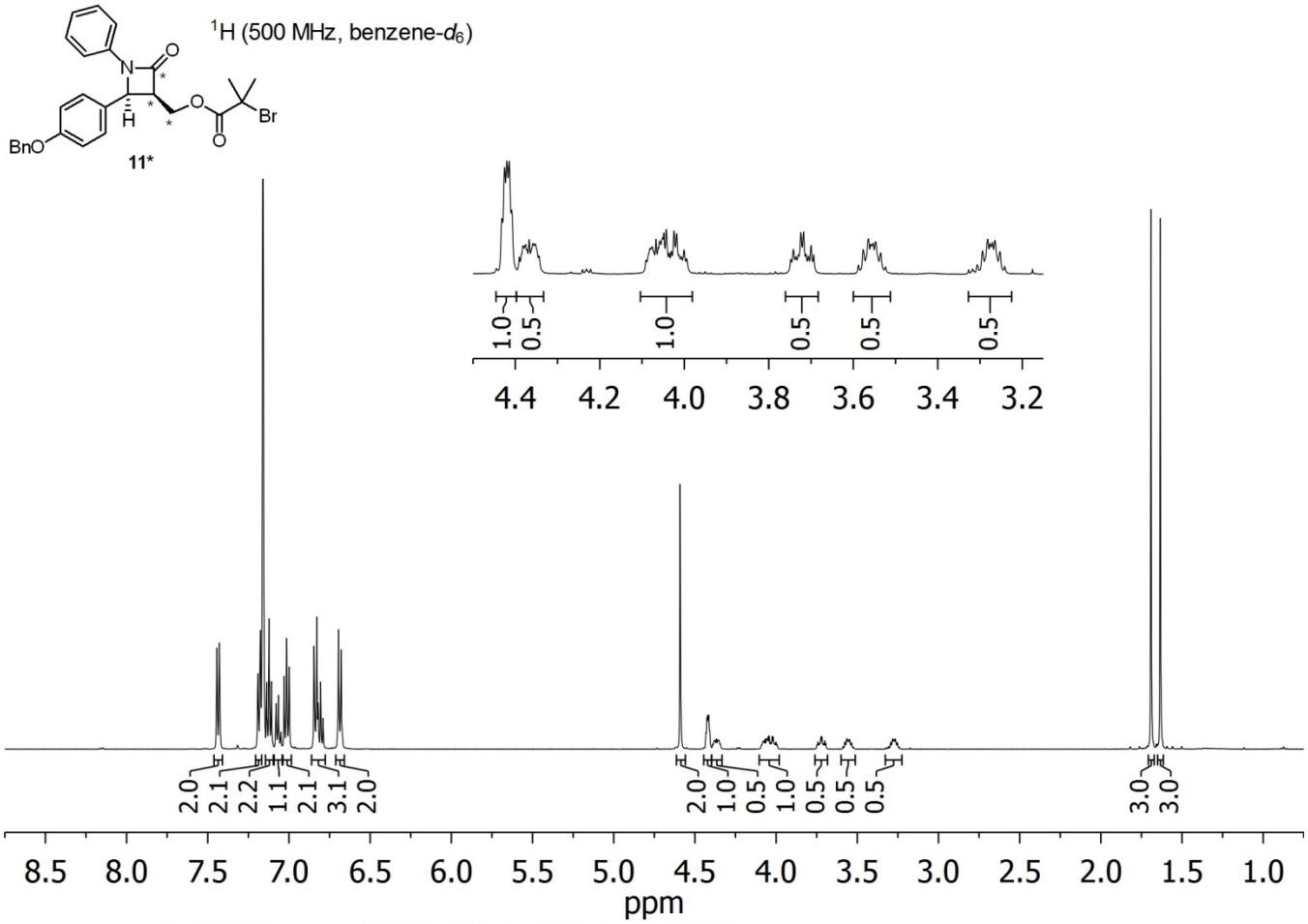
^{1}H (600 MHz, benzene-d_6)

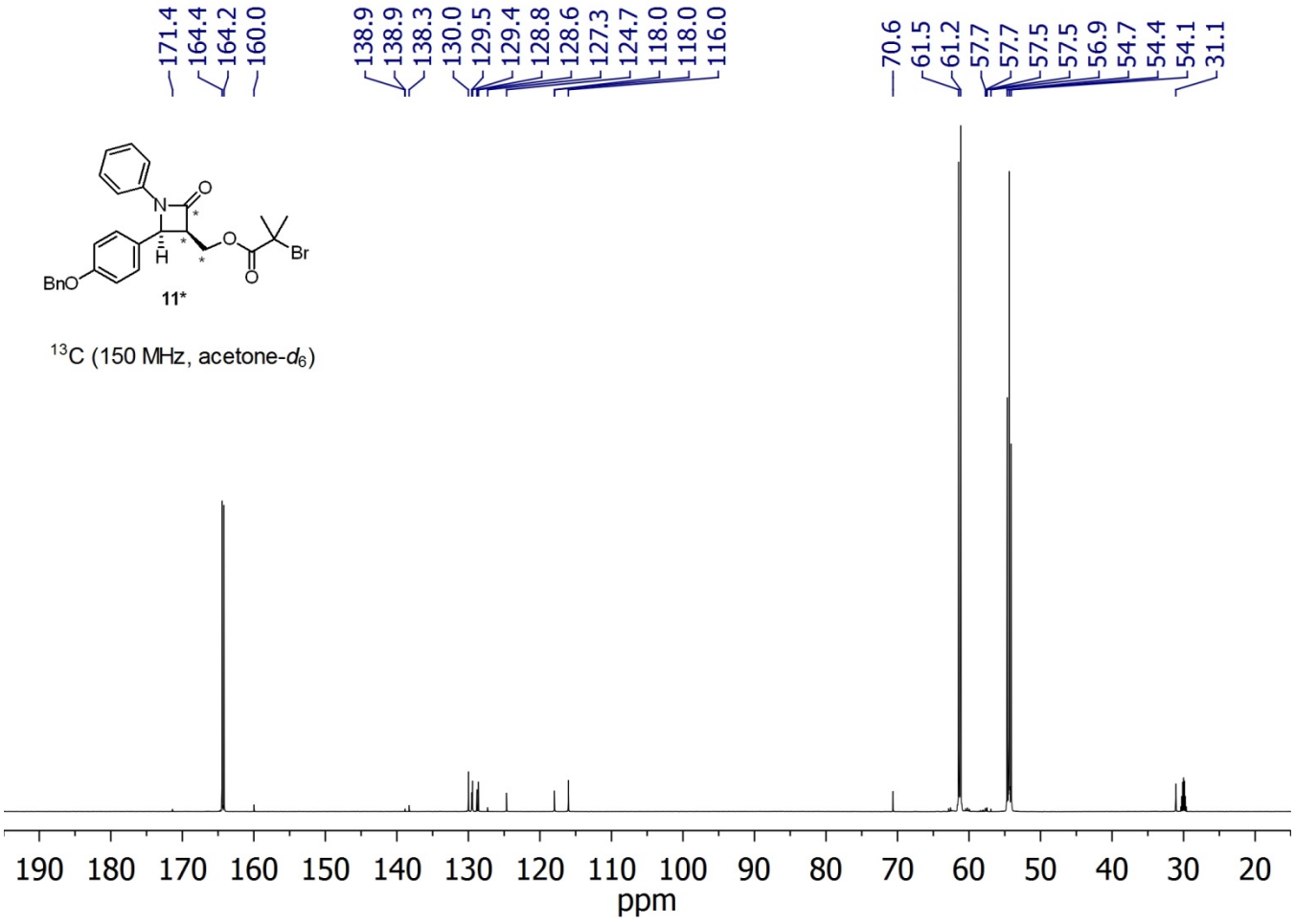




10*

^{13}C (150 MHz, benzene-d_6)


^{1}H (500 MHz, benzene-d_6)
11*
BnO
Br
ppm


171.4
164.4
164.2
160.0
138.9
138.9
138.3
130.0
129.5
129.4
128.8
128.6
127.3
124.7
118.0
118.0
116.0
70.6
61.5
61.2
57.7
57.7
57.5
57.5
56.9
54.7
54.4
54.1
31.1
11*
BnO
Br
^{13}C (150 MHz, acetone-d_6)
ppm